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THE RE-BREATHING TECHNIQUE

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The principle of deliberate re-breathing of anaesthetic atmospheres was introduced by McKesson in 1910 with the intention of conserving the gas in the end-inspiratory dead space which normally is of the same composition as the ambient atmosphere inhaled by the patient. Although the reason for the adoption of this method was primarily economic, McKesson pointed out that in addition 'as much gas containing CO_2 may be administered as desired',7 claiming, on the basis of work by Yandall Henderson, that this prevented the development of shock from acapnia which the rapid respirations of the anaesthetic state produced.

McKesson's unique anaesthetic machine was constructed with 'an adjustable graduated re-breathing bag by which the volume of gas breathed at each respiration may be measured, and by which any measured portion of this gas may be re-breathed at the following respiration'.7 This precise control of the volume of gas which is re-breathed is immensely important, for if the volume is too great, not only is there an increase in the CO2 content but there is also a decrease in the O₂ content of the gas inhaled by the patient. Both these factors are critical in the method of anaesthesia which Mckesson popularized, for precise control of the O2 content of the inhaled mixtures of N2O and Os was the point upon which the success or the failure of an administration pivoted. There is little doubt that the untoward effects of N₂O discussed so ably by Courville³ are due to anoxic anoxia, and that frequently the accidents and fatalities in patients held deliberately on gas mixture containing 10% or less of O2 by volume were due to decreases in the O2 tensions of the gas mixtures produced by excessive re-breathing.10 The hyperpnoea induced by hypoxia and hypercarbia would naturally increase the physiological dead space, further contributing to the unfavourable conditions.

Portability, the need for economy in anaesthetic gases, and provision for peak inspiratory flow rates, governed the design of the Magill attachment⁸ with its reservoir bag. In principle (see Fig. 1) there should only be re-breathing

of conserved gas in the end-inspiratory dead space when this attachment is correctly used. But while the McKesson apparatus provided for precise manual adjustment of the volume re-breathed, the Magill attachment (and all similar apparatus provided with a reservoir and using a constant rate of flow of fresh gas) relies, for control of the volume re-breathed, on alterations of respiratory volumes and of the rate of flow of fresh gas. An increase in the flow of fresh gas or a decrease in the respiratory ventilating volume will reduce the volume re-breathed and vice versa.

Measurement of the flow of fresh gas is obligatory in very many types of anaesthetic machine with which the Magill attachment may be used, in order to determine the proportion of oxygen that is being administered from the machine. The flow of fresh gas thus constitutes a variable which is directly under the control of the anaesthetist. An arbitrary rate of total flow is chosen for the majority of patients.

But the respiratory ventilating volumes are not under the control of the anaesthetist unless he is using artificial respiration. They vary from minute to minute in the same patient and, as a rule, they are never measured. In setting his arbitrary total flow of fresh gas for an individual patient the anaesthetist hopes that the patient's respiratory minute volume will not exceed it. Apparently basing their estimates upon normals of 11-14 breaths per minute and 500-600 ml. per breath for average adults at rest,² anaesthetic manuals recommend rates of total fresh gas flow between 5 and 8 litres per minute.

Molyneux and Pask⁹ have pointed out that ventilating volumes of 14 litres per minute and more are not uncommon during N₂O-O₂-ether anaesthesia. Indeed, the addition of the 'mechanical dead space' of the face-piece, connections and expiratory valve stock (often as great as 100 ml.) to the existing anatomical dead space of the patient, by reducing the effective alveolar ventilating volume must lead to hypercarbia. A decrease in alveolar ventilating volumes will reduce the efficiency of CO₂ wash-out from the alveoli,

and the resulting hypercapnia will lead to a compensatory increase in tidal volume or in rate or both. If the flow of fresh gas is not increased pari passu, the degree of re-breathing will in turn be further increased.

The depression of the respiratory centre by premedicating drugs and by anaesthetic agents may produce the extreme case where tidal volume is equal to dead-space vol-Under such conume. ditions (see Fig. 2) no oxygen reaches the blood and no CO2 can be excreted from the body except by the inefficient mechanism of 'diffusion respiration' described by Draper and Whitehead.4 The anaesthetized patient lies always between normal states and this extreme, and hardly ever (unless vigorous artificial respiration is practised) on the opposite or respiratory alkalotic side of Little wonder. normal. then, that anaesthetic

drugs have so long been accused of producing an acidosis. We have already reported that the failure to adjust for the widespread individual variations in respiratory minute volumes when the Magill attachment is used led to excessive re-breathing and accumulation of CO₂. At the proximal end of the Magil attachment a CO₂ content of 0·53 vols. was found when the flows of fresh gas were 8 litres per minute. In 2 experiments hyperventilation produced values of the order of 4 vols. CO₂ at this same sampling point. These experiments were conducted on unpremedicated conscious volunteers, breathing air; for the determination of CO₂ tensions in anaesthetic gas mixtures is very difficult, the more so since the molecular weights of N₂O and CO₂ are the same.

As the complex and expensive equipment for such estimations is not available to us, an indirect attempt to deduce an increase or a decrease in the CO_2 content of anaesthetic atmospheres has been undertaken. This study is based upon the assumption that, as alterations in CO_2 tension in the blood form the most delicate and efficient regulator of respiratory ventilating volumes, the measurement of such volumes under varying conditions might provide a clue to the CO_2 tensions. Planned as a comparative study only, the work is not intended to provide a qualitative or a quantitative measurement of CO_2 tensions in anaesthetic atmospheres.

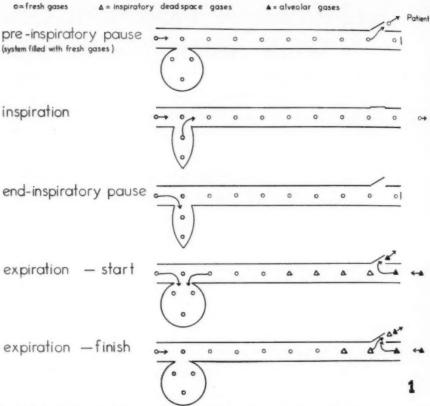


Fig. 1. Principle of the Magill attachment. If the total flow of the fresh gases is exactly equal to the respiratory minute volume, then, starting with the system filled with fresh gas, the patient will rebreathe only the conserved end-inspiratory dead-space gas, which is virtually fresh.

METHOD

Respiratory minute volumes were measured in 2 groups of patients receiving thiopentone-N₂O-O₂-ether anaesthesia for intra-abdominal operations, extra-abdominal operations and operations upon the head, neck and extremities. No selection was exercised beyond excluding any patient for whom the use of a muscle relaxant became necessary. Usual forms of pre-medication were employed.

In the first group the patients received the anaesthetic in a routine fashion from a Boyle's machine and Magill attachment. The rates of flow of fresh gas were held constant from start to finish at 2 litres per minute for O_2 and 6 litres per minute for N_2O . Thiopentone (2.5% solution) was used in divided intravenous doses to assist induction (see below).

In the second group a Gillies mark III machine was used. Unidirectional valves at the face-piece prevented any rebreathing. The Magill attachment was used to conduct gases to the patient, but the reservoir bag now could only accumulate fresh gases flowing from the machine during the expiratory phase. The gas flows were varied so that the reservoir bag was never more than one-third filled.

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This was done to prevent the flow of gas through the measur- NON REBREATHING ing system during the expiratory phase. The O2 content of the fresh gas was always held at 25% or more. Peak respiratory demands were met by permitting draw-over of air through the machine. The whole volume of the expiratory phase was exhausted to room air.

Gas volumes were measured with a Siebe-Gorman dryflow gas meter calibrated in one-tenth litres and litres and multiples thereof. This gas meter was inserted on the inspiratory limb of the circuit at all times.

As the schematic representations of the circuit demonstrate in Fig. 3, it was easy to insert the gas meter on the inspiratory side in the 'non-rebreathing group' but as the meter measures flow in one direction only, some adaptation was required to measure inspiratory volumes in the group on the Magill attachment. Here the unidirectional valves at the face-piece were also used, but the exhalations were led back to the Magill attachment at a point just distal to the expiratory valves. They were thus able to pass back towards the reservoir bag and escape from the valve in the usual way. As the unidirectional valves and flow meter were interposed between the expiratory valve and the facepiece but did not permit any re-breathing within their own circuit, their added volumes did not lead to any increase in the mechanical dead-space or in the volumes re-breathed. They did add fractionally to the resistance and they introduced a time lag, for the gas re-breathed was that which had been exhaled by the patient several breaths earlier.

In general the respiratory ventilating volumes were measured for the whole period of the anaesthetic and were subsequently divided by elapsed time in order to determine the mean respiratory minute volume. Since the metabolic rate, and hence the respiratory functions, is related more closely to surface area than to height alone or weight alone, the mean respiratory minute volume was in turn divided by the patient's surface area (derived from height and weight

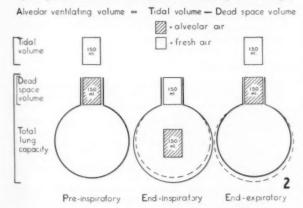
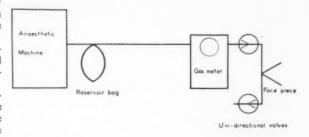


Fig. 2. Effective pulmonary ventilation. End-inspidead-space air is fresh air and is exhaled as such. End-inspiratory Endexpiratory dead-space air is alveolar air and is re-inhaled unchanged in composition. Thus the dead-space air does not affect the composition of alveolar air. To determine the volume of gas which adds oxygen (or anaesthetic) to, and receives CO₂ from, alveolar air, the dead-space volume must be subtracted from the tidal volume. Multiply by rate to determine the effective ventilation per minute. In this example tidal volume is equal to dead-space volume and alveolar



MAGILL ATTACHMENT

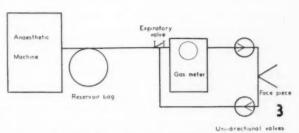


Fig. 3. Gas Flow Diagrams. Upper: Non-rebreathing circuit. Lower: Circuit for the Magill attachment.

by reference to an appropriate table1) and the resultant was expressed in terms of litres of gas per square metre of body surface area per minute (l./sq.m./min.).

It was originally intended to use a N2O-O2-ether technique only, but the first attempt to achieve this with the nonre-breathing circuit underlined very graphically the reason for the popularity of the McKesson 'fractional re-breathing technique' and the Magill attachment. It served also to strengthen the validity of the assumption on which this study was based and it emphasized the work of Haggard⁵ on the importance of the volume of breathing during the induction of ether anaesthesia. Without the respiratory stimulation which the re-breathing of exhaled CO₂ provided, it proved almost impossible to induce anaesthesia with N₂O-O₂-ether within a reasonable period of time. use of thiopentone to assist the induction of anaesthesia with the non-re-breathing technique became obligatory and, to balance the groups, the use was extended to all patients. The total dose of thiopentone seldom exceeded 500 mg. and the maximum used in any single patient was 700 mg. over a period of 21 hours. With the assistance of thiopentone the non-re-breathing technique provided very satisfactory anaesthesia and excellent muscular relaxation in light planes of anaesthesia. A gastric resection was one of the operations performed under this form of anaesthesia.

RESULTS

The results are set out in Table I. It must again be emphasized that this work was undertaken as a comparative

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study. The flow-meters on the Boyle and Gillies anaesthetic machines were not re-calibrated to determine their accuracy, nor was the gas meter. Because in clinical anaesthesia the anaesthetist must depend upon the patient for information concerning his height and weight or else estimate these

TABLE I. PULMONARY VENTILATION DURING CLINICAL ANAESTHESIA

	Non-Re-breathing Group	Magill Attachment Group (8 L/Min. fresh gas flow)
Mean Ventilating Vol- umes (in litres per square metre of body surface per minute)	4·18±1·80	5·62±2·24
Number of subjects Age range (years) Height range (inches) Weight range (lb.)	23 13-86 58-72 95-300	15-75 58-74 95-195

All subjects received routine pre-anaesthetic medication and were scheduled for elective operations.

parameters, the latter practice was followed. Although checks usually proved the guesses to be not more than 1 inch or 2-3 lb. below or above the actual figures, the error in these data is probably of the order of 2 inches and 5 lb.

The mean respiratory ventilating volume for the 'nonre-breathing' group was 4.18 ± 1.80 l./sq.m./min. corresponds closely to the average resting value of between 3 and 4 l./sq.m./min. for normal adult men which is quoted by Comroe.2 It suggests that the respiratory depression produced by the pre-medicating and anaesthetic drugs is approximately cancelled by the respiratory stimulation which increase of dead-space (by the addition of the mechanical dead-space of the face-piece) normally produces.

The mean respiratory ventilating volume for the 'Magill attachment' group was 5.62±2.24 1./sq.m./min. represents an increase of 34% over the mean for the 'nonre-breathing group', and suggests that, after the effects of the added mechanical dead-space and of drug-induced alterations to respiration have been allowed for, there is a large increase in ventilating volumes. We feel that this increase is almost certainly due to an increase in the CO2 content of the anaesthetic atmosphere arising from accumulation of exhaled gas other than the end-inspiratory dead-

While the increase in CO2 is of technical value in the induction of anaesthesia with N2O-O2-ether it must be remembered that it is a product of 2 variables, the flow of fresh gas and the respiratory minute volume. Unless the former, which is under the control of the anaesthetist, is held approximately equal to the latter, CO2 may accumulate to toxic levels.

SUMMARY

Unless precisely controlled, re-breathing of anaesthetic atmospheres may lead to hypoxia and to accumulation of

In an attempt to deduce the presence or absence of CO, in anaesthetic atmospheres without recourse to elaborate and costly instruments, comparative studies were undertaken on 2 groups of patients during clinical anaesthesia.

Respiratory minute volumes measured in the group anaesthetized by means of the Magill attachment with rebreathing were 34% greater than those for the group anaesthetized by means of a 'non-re-breathing' technique.

It is felt that this indicates a considerable degree of CO2 accumulation during the use of the Magill attachment when an arbitrary total flow of 8 litres of fresh gas per minute is administered to the patient.

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DIE BEREKENING VAN AFSKEIDING IN DIE MAAG

As 'n mens nie besef hoe beperk die hedendaagse toetse vir maagafskeiding is nie, kan jy maklik versink in 'n moeras van onbruikbare antwoorde. 'n Paar jaar gelede was die patroon van die fraksionele toetsmaal as baie belangrik beskou, maar vandag weet ons dat hierdie patroon van dag tot dag kan wissel en dat dit amper nie die moeite werd is om die toets uit te voer nie. As ons wil vasstel wat die maag se vermoë tot die afskei van soutsuur is, is daar slegs twee vrae wat die aandag verdien: kán dit soutsuur afskei en, indien wel, hoeveel?

Daar is twee siektetoestande waarby 'n mens moet weet of die maag in staat is om HCl af te skei, nl. megaloblastiese anemie en vermoede peptiese verswering. praktiese doeleindes beteken die aanwesigheid van vrye soutsuur dat kwaadaardige bloedarmoede uitgeskakel kan word en, mits 'n doeltreffende prikkel gebruik word, sluit sy afwesigheid die bestaan van 'n peptiese seer uit. Indien histamien toegedien word in 'n dosis van 0.4 mg. op 10 kg. liggaamsgewig (d.w.s. viermaal meer as die gebruiklike hoeveelheid), reageer die wandstandige selle maksimaal, en skei die maag soveel suur af as wat dit maar kan. Hierdie "versterkte histamientoets'1 kan heel moontlik heeltemal die plek inneem van die fraksionele toetsmaal. Ongewenste newe-effekte kan voorkom word deur voorafgaande toediening van mepiramien waterstofmaleaat (anthisan') wat, merkwaardig genoeg, nie die maag se reaksie beïnvloed nie.

Daar is geen besondere nut van die ander afskeidingstimuleerders nie—die meeste is dan ook baie swakker as histamien. Insulien het 'n kragtige uitwerking, maar 'n mens weet nie of hy as prikkelmiddel geslaag het tensy jy kan bewys dat hipoglisemie op die toediening daarvan eavolg het nie 2

Die versterkte histamientoets is ook al gebruik by kwantitatiewe berekenings van maagafskeidings. Soos verwag kan word, is groot hoeveelhede aangetref by gevalle van dundermsere, en normaal tot klein hoeveelhede by pasiënte met maagsere.¹ Marks³ het met die toepassing van hierdie toets aangetoon dat daar 'n sterk korrelasie is tussen die hoeveelheid suur wat afgeskei word en die aantal wandstandige selle. Mense wat gans te veel afskei is veral onderhewig aan maagverswering ná gastrektomie, en Marks doen aan die hand dat afskeiding in groot hoeveelhede 'n aanduiding is dat 'n uitgebreide maaguitsnyding nodig is.⁴

Dit sou gewens wees om buisinsetting in die maag te vermy, as 'n mens seker kon wees dat dié metode net so betroubaar is as die versterkte histamientoets. Ons het onlangs die "Diagnex-A'-toets bespreek, wat berus op die loslaat van 'n kleurstof (asure A) uit 'n ioon-uitruilende hars in die aanwesigheid van vry H+-ione, en sy daar-

EDITORIAL

THE ASSESSMENT OF GASTRIC SECRETION

Unless one realizes the limitations of the tests of gastric secretion in current use, one is likely to get bogged down in a morass of useless answers. Some years ago much attention was paid to the pattern of the fractional test meal, but we know now that this may vary from day to day and that the test is hardly worth performing. In testing the capacity of the stomach to secrete hydrochloric acid, only two questions are worth considering—can it produce acid, and if so, how much?

There are two conditions in which one needs to know whether or not the stomach can secrete HCl, megaloblastic anaemia and suspected peptic ulceration. For practical purposes the presence of free HCl rules out pernicious anaemia and, provided an adequate stimilus is used, its absence excludes a peptic ulcer. If histamine is given in a dosage of 0.4 mg. per 10 kg. body-we1g1 t (i.e. four times the usual amount), the parietal cells respond maximally, and the stomach secretes as much acid as it is capable of producing. This 'augmented histamine test' might well replace the fractional test meal. Undesirable side-effects are prevented by the prior administration of mepyramine hydrogen maleate ('anthisan') which, strangely enough, does not affect the gastric response.

There is no special merit in using other secretogogues, most of which are far weaker than histamine. While insulin has a powerful action one does not know whether or not it has achieved its stimulatory effect unless one can show that hypoglycaemia was induced.²

The augmented histamine test has also been used in quantitative studies of gastric secretion. As might be expected, high levels have been found in cases of duodenal ulcer and normal-to-low figures in patients suffering from gastric ulceration. Using this test Marks has shown a good correlation between the acid output and the number of parietal cells. Gross hypersecretors are especially liable to stomal ulceration after gastrectomy and Marks suggests that a high level of secretion indicates the need for an extensive gastrectomy.

The avoidance of gastric intubation would be desirable if one could be sure that the method was as reliable as the augmented histamine test. Recently we commented upon the 'Diagnex-A' test, which depends upon the release of

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opvolgende opname en uitskeiding in die urine.5 Indien hierdie ,buislose' toets aantoon dat suur uitgeskei word, kan kwaadaardige bloedarmoede uitgeskakel word, maar die toets het nie juis enige ander waarde nie.

Anders as die ,Diagnex-A'-toets, word resultate behaal met die berekening van die kwantitatiewe urien-6 en bloedpepsinogeen.7 Pepsinogeen word grootliks in die binneruimte van die maag afgeskei, maar 'n klein hoeveelheid kom endokriengewys in die bloedsomloop te lande en word deur die niere uitgeskei. Die urien- en bloedgehaltes is baie laag ná algehele maaguitsnyding of by kwaadaardige bloedarmoede, en is geneig om hoog te wees by pasiënte met dundermsere. Daar is reeds baie maal gebruik gemaak van die pepsinogeen-inhoud van urienmonsters versamel oor 8 periodes van 24 uur elk, maar kwantitatiewe versamelings is lastig en urienchromogene stuur dikwels die kleurmeterbevindings in die war;6 die berekening van serum-pepsinogeen word dus tans meer gewild. Monsters kan sonder oponthoud verkry word; dis 'n maklike metode, en die resultate kan herhaal word.8 Daar is 'n redelike korrelasie tussen serumpepsinogeengehaltes en die maag se suurproduksie, maar dit is nie afdoende nie en geld nie by lae afskeidingshoogtes nie;9 die toets is dus nie heeltemal bevredigend nie.

Die soektog op 'n eenvoudige en betroubare metode om die maagafskeiding te bereken gaan dus voort. Binne goedbepaalde grense sal die ontdekking van so 'n metode baie waardevol wees by 'n groot verskeidenheid probleme in die kliniek en in die navorsing.

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- a dye (azure A) from an ion-exchange resin in the presence of free H+ ions and its subsequent absorption and excretion in the urine.5 If this 'tubeless' test shows that acid is excreted, pernicious anaemia may be ruled out, but it has little other value.
- Unlike the 'Diagnex-A' test, measurement of the urinary^a and blood⁷ pepsinogen gives quantitative results. Pepsinogen is largely secreted into the gastric lumen, but a small proportion enters the circulation in endocrine fashion and it is excreted by the kidneys. The urinary and blood levels are very low after total gastrectomy or in pernicious anaemia and tend to be high in patients with duodenal ulcer. The measurement of the pepsinogen content of samples of urine collected over eight 24-hour periods has been much used, but quantitative collections are cumbersome and urinary chromogens often interfere with colorimetric readings8 so estimation of the serum pepsinogen is becoming more popular. Samples are instantaneously obtained, the technique is easy and the results are reproducible.8 There is a reasonable correlation between serum-pepsinogen values and the gastric acid output, but this is not absolute and does not hold at low levels of secretion, so the test is not completely satisfactory.

The quest for a simple and reliable method of assessing gastric secretion continues. Within well-defined limits the discovery of such a technique would be of great value in a variety of clinical and research problems.

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ETIOLOGIE VAN SWANGERSKAPSTOKSEMIE

ONDERSOEK NA 'N ANTIDIURETIESE POLIPEPTIED IN DIE URINE*

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met tegniese hulp van

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Die oorsaak van swangerskapstoksemie is nog onbekend, maar daar is heelwat feite bekend wat op die oorsaak betrekking mag hê, en op grond waarvan verskeie aantreklike teorieë al voorgestel is. Ons huidige kennis kan onder die volgende hoofde benader word: (1) Ischemie van die uterus en/of plasenta, (2) verstoorde nier-metabolisme, (3) die rol van dieet, (4) verstoorde sout- en watermetabolisme, en (5) endokriene-veranderinge.

Ischemie van die uterus en/of plasenta

Dit is welbekend dat toksemie meer dikwels voorkom in gevalle van eerstelingswangerskappe, tweelinge, hidramnios,

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verborge abruptio placentae, ens., waar 'n verhoogde binnebaarse druk veronderstel word om te lei tot relatiewe plaaslike ischemie met afskeiding van metaboliese gifstowwe in die sirkulasie, of refleks nierischemie met 'n ,kwaadaardige kringloop',1, 2

Bastiaanse en Mastboom3 in Amsterdam het in honde die aorta benede die nierslagare, of die arteria uterinae afgebind. In swanger honde het die daaropvolgende baarmoederischemie sonder uitsondering 'n styging in bloeddruk tot gevolg gehad, terwyl in nie-swanger diere geen sulke effek waarneembaar was nie.

In die mens het eksperimente om te bewys dat bloedsomloop in die uterus en plasenta verminder is in toksemie-gevalle,

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nog slegs indirekte gevolgtrekkings tot vrug gehad. Walker en Turnbull⁴ van Aberdeen het die suurstofversadiging in die naelstringbloed van foetusse deur keisersnee of histerotomie verlos, ondersoek en gevind dat dit geleidelik val na die 32ste week, en kenmerkend meer so in gevalle van toksemie. Klinies sien ons tekens hiervan in die welbekende verskynsels dat hierdie foetusse geneig is om te sterf in utero of tekens van nood te toon in kraam.

Morris et al.⁵ het 'n studie gemaak van die verwydering van radio-aktiewe sout uit die bloed nadat dit deur die buikwand in die uterusspier ingespuit is, en kon interessante bevindings publiseer: in normale swangerskappe het dit 4·1 minute geduur om radio-aktiwiteit tot die helfte te verminder; in gevalle van matige toksemie 7·7 minute en in hewige toksemie 15·3 minute. Hul het ook getoon dat behandeling met hipotensiewe middels 'n verbetering getoon het in die snelheid van verwydering van die radio-aktiewe sout.

Assali⁶ het ook bewys dat die bloedsomloop in die uterus, nier en brein verminder is in gevalle van toksemie, en dat toediening van Apresoline dit verbeter.

Verstoorde nier-metabolisme

Voorheen is gemeen dat daar definitiewe morfologiese veranderinge voorkom in die toksemiese nier, maar Govan⁷ het getoon dat daar geen histologiese verskille is tussen die niere van vroue wat sterf aan toksemie, en dié wat sterf aan ander oorsake op 'n ooreenstemmende stadium van swangerskap nie.

Kenney et al.⁶ en Assali et al.⁶ in die mens, en Parry en Taylor⁶ van Oxford, in skape, het egter getoon dat daar baie definitiewe funksionele veranderinge in die toksemiese nier voorkom, en 'n indrukwekkende ooreenkoms tussen die bevindinge in die mens en die skaap is getoon. Ook van groot belang is dat die bevindinge dieselfde was in skape wat spontaan toksemie ontwikkel het, sowel as in dié waar toksemie eksperimenteel induseer was op 'n eenvoudige dog miskien etiologies baie betekenisvolle wyse, hiervan later.

Die belangrikste funksionele veranderinge is (1) verlaagde nier-bloedsomloop, (2) verlaagde glomerulus-filtrasie, (3) verlaagde ureum- en kreatinien-uitskeiding, (4) verlaagde urinêre ureum-konsentrasie, en (5) verhoogde bloedureum en plasmakreatinien

In skape is laasgenoemde drie bevindinge mees merkbaar, wat nie in die mens die geval is nie. In skape is water-retensie met edeem nie so algemeen as wat in menslike toksemiegevalle voorkom nie.

Die rol van dieet

Algemeen gesproke, kom toksemie meer dikwels voor by arm en ondervoede bevolkingsgroepe, byvoorbeeld in die Ooste, en veral waar daar 'n tekort aan die vitamine-B kompleks in die dieet is. Eksperimente soos die Toronto en dié van die People's League of Health wat sowat 15 jaar gelede uitgevoer is, het ook getoon dat in groepe waar 'n goeie gesupplementeerde dieet aangebied was, die voorkomssyfer laer was as in die kontrole-groepe.

Wat egter in die lig hiervan verbasend was, was die lae voorkomssyfer in lande op die vasteland van Europa waar hongersnood geheers het gedurende die laaste wêreldoorlog, en die skielike hoë voorkoms van eklampsie in Holland, net nadat voedselvoorrade per valskerm afgegooi is deur die Geallieerdes in die lente van 1944, na 'n periode van verhongering.

Dit bring ons by onlangse eksperimentele werk op skape

wat deur Parry¹⁰⁻¹² in Oxford gedoen is, en waarmee hy nog voortgaan.

In skape is daar naamlik ook 'n toksemie van swangerskap wat tot onlangs in sekere troppe in die laelande van Brittanje 'n 20-25% mortaliteit in sekere seisoene gedra het, veral na strawwe winters maar ook in heel gewone seisoene: Die kondisie staan ook bekend as ,tweeling-lam siekte' omdat geaffekteerde ooie byna altoos tweelinge of drielinge dra. In die hoëlande van die Verenigde Koninkryk is dit skaars, en interessant genoeg dra die ooie daar baie minder tweelinge. Die rede meld Parry nie in sy geskrifte nie, en is my onbekend.

Hy het egter gevind dat in 'n potensieel vatbare ooi, enige skielike verandering in die hoeveelheid of kwaliteit van die voedsel, ôf te veel na 'n periode van verhongering, ôf verhongering na geil voeding, die siekte tot stand mag bring, veral as daar eers tekort was aan goeie proteïne. In sy laboratorium het hy gevind dat 4 uit 5 ooie so reageer. Deur oordeelkundige voedingsvoorskrifte het hy en sy helpers in verskeie troppe in die laelande die voorkoms- en sterftesyfers bemoedigend verminder, en reken dat laasgenoemde tot 2% (vanaf 20-25%) en die voorkomssyfer tot 5% afgebring kan word.¹²

Waarnemings oor dieet-toesig in swangerskap in die mens het die tot dusver mees dramatiese verbetering in die voorkomssyfer van toksemie en eklampsie teweeggebring, naamlik in die werk van Hamlin^{13, 14} by die Women's Hospital in Sydney. Sy werk is gestimuleer deur dié van Dieckmann et al.15 in Chicago, wat getoon het dat pasiënte wat erge toksemie ontwikkel, reeds by die 13de week van hul swangerskap oormatig in gewig begin toeneem het. Hul het daarop gestaan dat nie meer as 8 lb. in die 10 weke vanaf die 20ste tot die 30ste weke behoort opgetel te word nie. Australiërs wat onder Hamlin gewerk het, het my vertel dat wanneer een van die geneeskundiges op 'n dag by die voorgeboortelike kliniek miskien nie sou opgelet het dat 'n vrou byvoorbeeld 5 lb. binne 14 dae opgetel het nie, Hamlin hom goed die ore sou gewas het en dan die pasiënt met sy eie motor by haar huis gaan haal het! So 'n pasiënt is dan onder streng dieet-toesig geplaas. Koolhidrate en sout is beperk; proteïne, groente en vrugte in voldoende hoeveelhede toegelaat. Die pasiënt is nie ontslaan voordat sy haar dieet en die belangrikheid daarvan verstaan het nie, haar oormatige gewigstoename gekorrigeer is en seker gemaak is dat verdere tekens van toksemie nog nie hul verskyning gemaak het nie.

Hierdie sienswyse kry vandag meer en meer wêreldwye aanhang, en baie verloskundiges glo nie alleen dat oormatige gewigstoename die eerste teken van dreigende toksemie is en die ontwikkeling van hipertensie, edeem en albuminurie voorafgaan nie, maar ook dat die voorbehoeding daarvan in die meeste gevalle toksemie kan verhoed, en sekerlik verhoed dat dit ernstige afmetings aanneem.

Dit mag wees dat die prysenswaardige resultate van Hamlin slegs te danke is aan die spesiale aandag en strenge toesig wat sy pasiënte kry. Hoe dit ookal sy, vanaf 1936 tot 1947 was die voorkomssyfer vir eklampsie by die Women's Hospital in Sydney 1/350 gemiddeld. In 1948 het hy met sy prosedure begin, en die voorkomssyfer het dadelik begin val. In 1951 was dit 1/7000! Die voorkomssyfer vir pre-eklamptiese toksemie het geval van 10% tot 1·8%.

Sover aangaande oormatige gewigstoename. Is daar in die mens enige getuienis dat veranderinge in die kwaliteit van dieet, of seisoensveranderinge, 'n rol mag speel soos in skape? Myns insiens mag daar wel wees. Hier by ons in Suid-Afrika is die hoogste voorkomssyfer vir toksemie in die lente (einde September tot begin Oktober). In Brittanje is dit in die ooreenstemmende seisoen (einde Maart tot begin April). Kan dit nie wees dat in die wintermaande 'n tekort aan groente, vrugte en proteïne teweegbring dat te veel stysel geëet word deur verwagtende moeders wat dan juis by daardie belangrike twintigste tot dertigste weke is en juis nie 'n styseldieet wat oormatige gewigstoename mag meebring, behoort te nuttig nie? Wanneer die lente dan volg, is hierdie vroue by die dertigste tot agt-en-dertigste weke van hul swangerskap, waar die hoogste voorkomssyfer vir skielike ontwikkeling van hewige toksemie en eklampsie gevind word. Mag dit nie wees as gevolg van dieetverandering wanneer die lentevoorraad goedkoper groente op die mark kom nie?

Hoe beïnvloed gewigstoename dan die ontwikkeling van toksemie? Chesley¹⁶ het kategories dit so gestel dat vroue wat 'n skielike abnormale gewigstoename toon, besig is om water op te gaar. Daar is dus blykbaar 'n verstoring van sout- en watermetabolisme.

Verstoorde sout- en watermetabolisme

Sedert Zangemeister¹⁷ in 1915 die ontwikkeling van toksemie probeer verklaar het op grond van die opgaring van oormatige vloeistof in die liggaam, is al baie pogings gemaak om hierdie teorie te probeer bevestig. Dit is moontlik dat in sommige gevalle toksemie en eklampsie hul kliniese tekens te wyte het aan die opgaar van 'n oormaat water, heelwaarskynlik as gevolg van die terughouding van te veel sout. Hierdie veranderinge in sout- en watermetabolisme mag weer te wyte wees aan ander verstorings van onbekende aard, heelwaarskynlik endokrien, en moontlik soos reeds getoon, aan kwantitatiewe of kwalitatiewe dieetveranderinge.

Kliniese edeem is 'n algemene maar nie noodwendige teken van toksemie nie. 'n Mens sien dikwels gevalle met oormatige gewigstoename plus hipertensie en selfs albuminurie, sonder edeem. Dieckmann¹8 het gevind dat pasiënte met toksemie vererger kan word (hul hipertensie, albuminurie en edeem vermeerder) deur die toediening van 2·5% soutoplossing binneaars. In 30% van sy gevalle het tekens van dreigende eklampsie ontwikkel, maar in ander is die sout en water snel deur die niere uitgeskei, met slegs tydelike waarnemings van verergerde toksemie. Opgaar van sout en water is dus nie al nie, en het nie dieselfde effek of betekenis in elke pasiënt nie.

Die edeem van 'n toksemiese pasiënt kan verminder word deur strenge beperking van soutinname, maar dit moet streng wees om effektief te wees. Hierdie maatreëls plus 'n paar dae in die bed op die regte tyd kan dikwels die bordjies verhang en 'n dreigende toksemie tot ommekeer bring na 'n groot diurese, selfs in soverre dat 'n gevaarlik hoë bloeddruk en in uitsonderlike gevalle selfs albuminurie kan tot normaal terugkeer, of ten minste soveel verbeter dat met die swangerskap aangegaan kan word tot die foetus groot genoeg is om 'n redelike kans op oorlewing te hê. Die vermindering van edeem is ook belangrik in die voorbehoeding van eklampsie, deurdat serebrale edeem veronderstel is om die prikkelbaarheid van die korteks te verhoog.

Die gebruik van Diamox (Lederle) beide in die voorbehoeding sowel as in die behandeling van toksemie word tans ondersoek. Die uitwerking is deur die inhibisie van die karbonies-anhidrase ensiem in die nier, as gevolg waarvan meer bikarbonaatsout in die urine uitgeskei word. Die sout neem water saam, en terselfdertyd word die urine alkalies.

Endokriene-veranderinge

Die voorste lob van die pituitêre klier groei gedurende swangerskap tot tweekeer sy normale grootte, en 'n mens verwag 'n verhoogde produksie en tekens van vermeerderde aktiwiteit van sy hormone.

Die byniere groei ook merkbaar, en die uitskeiding van die bynier-hormone of kortikoïedes in die urine is verhoog. Die uitwerking van ACTH—sout- en waterretensie en hoë bloeddruk—is indrukwekkend baie soos die prentjie van toksemie. Swangerskap is al beskryf as 'n ,fisiologiese Cushing-sindroom', en die vergelyking is van toksemie natuurlik nog veel meer waar. Venning¹9 het bevind dat in toksemie die konsentrasie van die bynier-glukokortikoïedes gelykstaan aan dié in Cushing, en Tobian²0 het getoon dat die formaldokortikoïedes styg rofweg parallel met die graad van edeem

Die voorstanders van 'n endokriene-etiologie vir swangerskapstoksemie het dus 'n aantreklike teorie, naamlik dat emosie of vrees, veral in 'n eerstelingswangerskap, 'n ,alarmreaksie' mag teweegbring, met die afskeiding deur die voorste lob van die pituitêre klier van verhoogde hoeveelhede ACTH, abnormale groei van die byniere, en die totstandkoming van 'n Cushing-agtige sindroom, toksemie.

Nog 'n effek van ACTH is verhoogde uriensuur-uitskeiding, en verhoogde bloed-uriensuur is een van die uitstaande biochemiese veranderinge in eklampsie.²¹

Martin en Mills²² het aldosterone-uitskeiding in normale en toksemiese swangerskappe bestudeer, en bevind dat daar 'n verhoogde uitskeiding in normale swangerskappe is, moontlik volgens hulle om die natriumuitskeiding-effek van progesteroon teë te werk. Vir toksemie was die syfers binne dieselfde perke as dié vir normale swangerskappe.

Dit mag betekenisvol wees dat, hoewel ongeveer 50 gevalle van swangerskap in vroue met Addison se siekte al beskryf is, klaarblyklik nie een toksemie ontwikkel het nie.²³ Baie interessant ook was die bevindinge van Ferebee *et al.*²⁴ wat 13 gevalle van Addison se siekte behandel het met desoksikortikosteroon, met 'n indrukwekkende sout- en waterretensie, vermindering in urine-afskeiding, edeem in 10 van die 13, en verhoging van die bloeddruk vanaf die lae lesings kenmerkend van Addison tot normaal in alle gevalle en tot hipertensie in 3.

Nie alleen die voorste lob van die pituitêre klier nie, maar ook die agterste lob het al navorsers wat soek na die oorsaak van toksemie geïnteresseer. Dit is algemeen bekend dat die ekstrak-preparate van dié klier 'n drievoudige effek het, naamlik vasopressor, antidiureties en oksitosies. Die teorie van Anselmino en Hoffmann²⁵ van Düsseldorf (1931) dat toksemie veroorsaak word deur abnormale aktiwiteit van die agterste pituitêre lob, was baie aantreklik, maar hul aanspraak op die teenwoordigheid van 'n antidiuretiese stof in die urine van toksemiese vroue is nie bevestig deur ander navorsers nie, tot onlangs weer indrukwekkende werk deur Arneil en Wilson²⁶ en Paterson²⁷ van Glasgow gepubliseer is. Eersgenoemdes het navorsing gedoen in die wyer veld van oligurie in die algemeen, en maak aanspraak daarop dat hul 'n antidiuretiese polipeptied in die urines van 'n wye verskeidenheid van oliguriese pasiënte geïsoleer het. Voorheen was dit aangeneem dat die oligurie in hierdie pasiënte aan parenchiemateuse veranderinge te wyte was. Paterson het die urines van vroue met toksemie, eklampsie, essensiële hipertensie en kroniese nefritis in swangerskap, sowel as van

norma papieren in wat or butano posisie poliper word of skeie in dieselfonorma bevat.

3 Mei

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normale swanger en nie-swanger vroue ondersoek met papier-chromatografie. Hy het in alle gevalle van eklampsie en in 15 uit 18 gevalle van hewige toksemie, 'n stof gevind wat op die chromatogram beweeg met fenol maar nie met butanol nie. Hierdie stof neem op die chromatogram 'n posisie in wat identies is met dié van die antidiuretiese polipeptied deur Arneil en Wilson beskryf. Dieselfde posisie word ook ingeneem deur 'n stof wat teenwoordig is in verskeie preparate van agterste pituitêre ekstrak wat ook op dieselfde manier deur Paterson getoets is. Slegs een van die normale urines deur hom getoets het hierdie stof skyn te bevat.

NAVORSING DEUR DIE SKRYWERS GEDOEN

Oor die afgelope 6 maande is 'n begin gemaak met soortgelyke chromatografiese studies op die urines van gevalle van toksemie van swangerskap in die Karl Bremer-Hospitaal, met die oogmerk om die bevindinge van Anselmino en Hoffmann en van Paterson te staaf, en hopelik meer uit te vind omtrent wat met die sogenaamde antidiuretiese polipeptied gebeur na behandeling van die toksemie en na verlossing. Ook het ons die urine van 3 manlike pasiënte, en 1 vrou, met die nefrotiese sindroom ondersoek, sowel as 3 verskillende kommersiële preparate van pituitrin, 3 van ACTH en 3 van kortisoon.

Die metode is kortliks as volg: 'n Katetermonster van urine word behandel binne 4 uur nadat dit geneem is. Die pH word gekorrigeer tot suur deur die byvoeging van asynsuur. Dan word 5 ml. gekook vir 10 minute in 'n waterbad by 100°C. Na afkoeling word dit filtreer om die eiwit te verwyder, en van die helder filtraat word 0.05 ml. as 'n kol in die een hoek van 'n 12-duim vierkant stuk Whatman No. 1 filtreerpapier geplaas. Dit word toegelaat om net droog te word, en dan word die een rand by die kol in waterversadigde fenol geplaas in 'n atmosfeer van ammoniak binne 'n lugdigte glastenk. Die fenol deurtrek die papier vanaf dié rand, en volgens die oplosbaarheid daarin van die verskeie aminosure in die urine, gaan elk van hulle vir 'n bepaalde afstand saam in 'n reguit lyn vanaf die kol. Dit neem ongeveer 15-18 uur vir die fenol om die papier tot by sy verste rand te deurweek. Dit word dan weer gedroog, gedraai deur 90 grade, en die ander rand by die kol word dan in butanolasynsuur geplaas, net soos met die fenol. Wanneer die papier hiermee deurweek is, word dit weer gedroog en daarna ontwikkel deur dit met ninhydrin te spuit en te bak in 'n

oond by 90-100°C vir 'n halfuur. Die verskillende aminosure verskyn dan in hul tipiese posisies as pers kolle. Dit is belangrik om die kolle te omlyn, want hul vervaag binne 'n dag of wat. Beste nog is om 'n fotografiese afdruk te maak (Fig. 1).

Die "antidiuretiese polipeptied' beweeg maksimaal met fenol, maar gladnie met butanol nie. Dié polipeptied was teenwoordig in 18 van ons laaste 21 gevalle van hewige toksemie, twyfelagtig in 1 geval, en afwesig in 2. Hierdie laasgenoemde 3 gevalle, net soos in Paterson se negatiewe gevalle, het weinig edeem gehad en was minder uiterste gevalle van toksemie (Fig. 2 en Tabel I).

In slegs 1 van 16 kontrole-urines geneem van vroue om en by 32-36 weke swanger sonder toksemie, is hierdie polipeptied gevind (Fig. 3). Dit bevestig ook Paterson se bevindings.

In al 4 gevalle van die nefrotiese sindroom was die polipeptied ook teenwoordig (Fig. 5), maar in een wat met kortisoon behandel is, was dit afwesig in 'n opvolg-chromatogram 10 dae na die aanvang van behandeling en nadat diurese plaasgevind het.

Die polipeptied was aanwesig in 2 uit 3 verskillende Pituitrin-preparate deur ons ondersoek (Fig. 5), maar die heel treffendste positiewe chromatogramme vir dié stof is verkry met die ACTH-preparate wat ons ondersoek het. Drie verskillende kortikotrofiese preparate het by herhaling 'n groot en duidelike polipeptied in die tipiese posisie ontwikkel (Fig. 6).

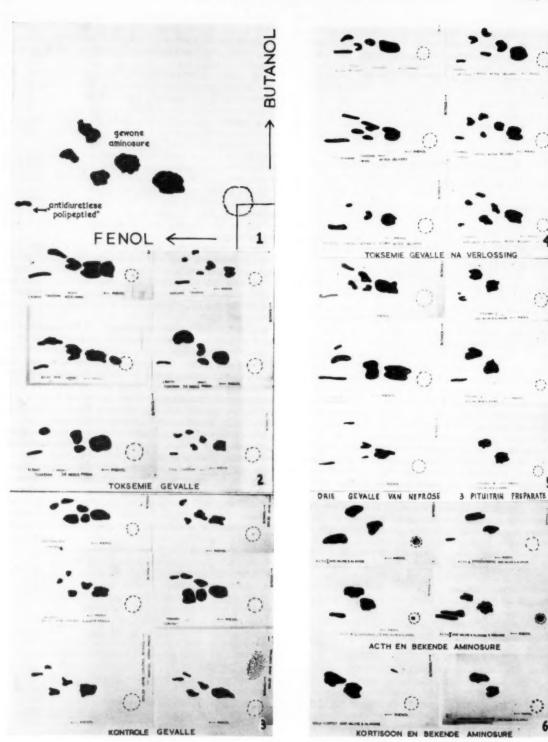
Die polipeptied was nie aanwesig in die chromatogramme van 3 verskillende kortisoon-preparate nie (Fig. 6).

Die chromatogramme gedaan op die urines van ons hewige toksemie-gevalle na behandeling en verlossing, het heel onverwagte resultate gelewer. Dit was verwag dat na diurese, verbetering in toksemie, en veral na verlossing, die 'antidiuretiese polipeptied' sou verdwyn. Dit was egter nie die geval nie. In alle gevalle van erge toksemie waar die polipeptied oorspronklik gevind is, en wat tot dusver opgevolg is (14 in getal) het die stof na behandeling en selfs na verlossing, met verdwyning van kliniese tekens van toksemie, in die urine teenwoordig gebly (Fig. 4).

Dit was moontlik om sommige gevalle langer as die puerperium op te volg. Tot dusver is 6 gevalle so opgevolg. In 2 gevalle was die polipeptied nog teenwoordig 3 weke na verlossing, in 2 na 6 weke, in 1 na 7 weke, en in 1 na 4 maande. In een van die 2 gevalle wat nog positief was na 3 weke, het die polipeptied egter verdwyn na 2 maande.

TABEL I. CHROMATOGRAFIE OP URINES VAN GEVALLE MET TOKSEMIE VAN SWANGERSKAP

							Polij	peptied			
Nommer	Ouderdom	Pariteit	Maturiteit (Weke)	Bloeddruk (mm. Hg)	Edeem	Eiwit	By Toelating	Na Behandeling en/of Verlossing	Opmerkings		
1	24	0	37	170/120	+	+++	Positief	Positief			
2	38	10	30	160/110	+++	+++	Positief	Positief	Mitr. sten. + toksemie.		
3	25	0	28	210/130	+++	Solied	Positief	Positief	Eklampsie.		
4	19	0	38	140/100	+++	++	Positief	Positief			
5	16	0	36	190/130	++	++	Positief	Positief			
6	22	0	39	160/100	Effe	++	Twyfelagtig		In kraam by toelating.		
7	26	1	34	180/120	Geen	Solied	Positief	Positief	Eklampsie.		
8	16	0	35	150/110	++	+++	Positief	Positief			
9	24 38 25 19 16 22 26 16 28 35 45 22 21 36 8 38	5	30 28 38 36 39 34 35 35 30 38 40 30 36 39 38	170/100	++++	Solied	Positief				
10 11 12 13 14 15 16 17 18	35	8	30	190/130	Effe	Solied	Positief	Positief			
11	24	2	38	150/100	Effe	Solied	Negatief				
12	45	12	40	215/130	++++	+++	Positief		Aksid. bloeding.		
13	22	1	30	210/120	+	++++	Positief	Positief	Chroniese nefritis.		
14	21	0	36	150/110	++	+++	Positief	Positief	Tweelingswangerskap.		
15	36	3	39	250/150	+	+++	Positief				
16	18	0	38	200/120	Geen	+++	Positief	Positief			
17	28	2	34	190/110	++	++	Positief	Positief			
		2	36	220/120	+	Solied	Positief		Verborge abruptio placentae. Anurie. Kortikale niernekrose. Dood.		
19	22	0	34	180/120	+++	++	Positief	Positief			
20	18	0	36	170/100	+	++	Negatief		In kraam by toelating.		
19 20 21	22 18 30	9	34 36 36	180/120	++	Solied	Positief	Positief	Eklampsie.		



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3 Mei

Watter bevind 'n P van vro is met polipel hierdie tied oo pituitê Oors

die po en (2) tot du hewige Indie toksem woordi vatbaa nie. N

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'n Pasiënt wat 'n histerotomie gehad het vir hewige toksemie op 30 weke voordat met hierdie navorsing begin is, is onlangs, 9 maande later, weer gesien vir 'n ginekologiese klagte. 'n Chromatogram is nou gedoen op haar urine, en was negatief vir die ,antidiuretiese polipeptied'.

GEVOLGTREKKINGS

Watter gevolgtrekkings kan ons dan maak van hierdie bevindinge?

'n Polipeptied is getoon teenwoordig te wees in die urines van vroue met hewige toksemie van swangerskap, wat identies is met dié beskryf deur vorige navorsers as 'n ,antidiuretiese polipeptied', en hul bevindinge is bevestig. Netsoos deur hierdie navorsers is in die huidige navorsing hierdie polipeptied ook geïsoleer in ekstrakte van die agterste lob van die pituitêre klier.

Oorspronklike bevindinge is (1) dat kommersiële ACTH die polipeptied bevat in oënskynlik baie sterk konsentrasie en (2) die polipeptied bly teenwoordig na verlossing vir 'n tot dusver onbekende tydperk, in die urine van vroue wat hewige toksemie gehad het.

Indien die polipeptied teenwoordig bly na alle tekens van toksemie verdwyn het, is die veronderstelling dat dit teenwoordig mag wees vóór toksemie ontwikkel, en 'n verhoogde vatbaarheid vir toksemie mag verteenwoordig, nie onvanpas nie. Navorsing om hierdie veronderstelling te bevestig sou vandag uiters moeilik wees. Met goeie voorgeboortelike sorg, veral kontrole van gewigstoename, is die voorkomssyfer van hewige toksemie in bespreekte gevalle feitlik nul. Die gevalle deur ons ondersoek was sonder uitsondering noodtoelatings of pasiënte wat versuim het om die kliniek by

Die teenwoordigheid van 'n antidiuretiese stof in vroue wat hewige toksemie gaan ontwikkel, daaraan onderhewig is, of dit gehad het, mag in die lig van die bevindinge van die huidige en vorige navorsers daarop dui dat oligurie met sout- en waterretensie en hoë bloeddruk die ontwikkeling van toksemie teweegbring onder die invloed van ACTH of die agterste lob van die pituitêre klier, of beide.

Klinies is al herhaalde waarnemings gemaak dat toksemiese pasiënte besonder sensitief skyn te wees vir posteriale pituitêre ekstrak.28, 29 Dit is ook bekend dat pasiënte met hewige toksemie geneig is om prematuur spontaan in kraam te gaan, of spoedig na induksie, suggestief van verhoogde oksitosiese aktiwiteit.

Die verhoogde sensitiwiteit vir die effek van pituitrin is deur verskeie skrywers toegeskryf aan die invloed van die gonadotrofiese hormone, al dan van pituitêre òf chorioniese oorsprong. Smith en Smith 30 het al in 1933 getoon dat daar 'n oormaat gonadotrofiese hormoon in die serum en urine van toksemiese vroue is, en later navorsers het bevestig dat dit wel waar is vir gevalle van hewige toksemie (soos dié deur ons ondersoek) maar nie vir matige toksemie nie.31

Dit word ook algemeen aangeneem dat beide oestrogeenen progesteroon-produksie verminder is in toksemie, wat weer suggestief is van ooraktiwiteit van die voorste lob van die pituitêre klier. Smith en Smith het die ovariale hormone gebruik in die behandeling en voorbehoeding van toksemie.

OPSOMMING

Hoewel die juiste etiologie van swangerskapstoksemie nog onbekend is, het uitgebreide navorsing in die laaste dekade baie feite aan die lig gebring wat regstreeks of onregstreeks op die etiologie betrekking mag hê, en na aanleiding waarvan aansienlike vordering reeds gemaak is, veral op die gebied van voorbehoeding en ook behandeling van die siekte.

Daar is getuienis dat oormatige gewigstoename of skielike dieetveranderinge, met sout- en waterretensie, etiologiese faktore mag wees, moontlik onder die invloed van endokrieneverstoringe, of oormaat ACTH van die voorste lob van die pituitêre klier, of oormaat antidiuretiese hormoon van die agterste lob, en miskien slegs in sekere pasiënte as gevolg van verhoogde sensitiwiteit onder die invloed van die gonadotrofiese hormone. Terselfdertyd is daar getuienis dat plasentaen nierischemie 'n rol speel. Die vermiste skakel is tussen die veranderinge in sout- en watermetabolisme, en dié in die plasenta- en nierfunksie. Hopelik sal entoesiastiese navorsing die skakel gou vind.

SUMMARY AND CONCLUSIONS

Although the exact cause of pre-eclamptic toxaemia of pregnancy is as yet unknown, extensive research over the past decade has brought to light many facts that may have direct or indirect bearing on the aetiology, as a result of which much progress has already been made, especially in respect of prophylaxis and also in the treatment of the disease. A review is given of current views on its aetiology.

There is evidence that excessive increase in weight or sudden dietary changes, with salt and water retention, might be aetiological factors, possibly under the influence of hormonal disturbances. These might be either excess ACTH of the anterior lobe of the pituitary gland, or excess antidiuretic hormone of the posterior lobe; perhaps in certain patients only they might be the result of increased sensitivity under the influence of the gonadotrophic hormones. At the same time there is evidence that placental and renal ischaemia are involved as trigger mechanisms and in establishing a vicious circle.

The present research is an investigation by two-dimensional paper chromatography into the presence of an antidiuretic substance in the urine of patients suffering from severe toxaemia of pregnancy. A polypeptide identical with that described as 'antidiuretic' by previous investigators 25-27 has been demonstrated in the urine in all but 3 out of 21 cases of severe toxaemia, and was present in only one of 16 controls. This polypeptide was also present in the urines of 1 female and 3 male cases of the nephrotic syndrome, and in 2 of 3 commercial posterior pituitary extracts.

The above findings confirmed those of previous investigators. Original findings were:

1. The 'antidiuretic polypeptide' was contained in apparently very high concentrations in 3 different commercial

Twee-dimensionele papier-chromatografie om die teenwoordigheid van 'n ,antidiuretiese polipeptied' te illustreer in die urine van pasiënte met toksemie van swangerskap, en in verskeie hormoon-ekstrakte.

Fig. 1. Verduidelikende chromatogram.

Fig. 2. Gevalle van toksemie—polipeptied teenwoordig.Fig. 3. Kontrole gevalle—polipeptied afwesig.

Fig. 4. Gevalle van toksemie na verlossing-polipeptied nog teenwoordig.

³ gevalle van nefrose-polipeptied teenwoordig. 3 Pituitrin ekstrakte plus bekende aminosure—polipeptied teenwoordig in 1 cn 2 afwesig in 3.

⁴ ACTH-preparate plus bekende aminosure—politeenwoordig. 2 Kortisoon-preparate en bekende peptied teenwoordig. aminosure--polipeptied afwesig.

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ACTH preparations; and was absent from 3 forms of cortisone tested.

2. The substance remained present for a variable period after delivery in every one of 14 cases of severe toxaemia upon whom follow-up chromatographic studies were made after clinical signs of toxaemia had resolved, and in some cases was still found to be present weeks or months afterwards. It is a conceivable assumption that it might be present before toxaemia develops, and might represent an increased liability in certain patients to develop toxaemia.

Ons wens die susters en verpleegsters van die kraamafdeling te bedank vir hul ywer in die neem van die kateter-monsters, en mnr. Neiteler, senior tegnikus, vir sy hulp met tegniese en fotografiese werk.

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OBSERVATIONS ON CONGENITAL HYPERTROPHIC PYLORIC STENOSIS*

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It has taken time to settle the controversy between the champions of medical and surgical treatment for congenital hypertrophic pyloric stenosis, and few now doubt that surgery provides a simple safe and expeditious relief of the pyloric obstruction. Rammstedt (1934) recorded that in his Dusseldorf experiment 92 cases were treated conservatively with a mortality rate of 18.8%, whereas the death rate for surgical treatment was 3.6% in 110 consecutive cases. Svensgaard (1925) used Eumydrin (atropine methyl nitrate) in 179 cases, the mortality rate was 5.5%. Tallerman (1951) treated 67 cases with a 0.6% alcoholic solution of eumydrin, using 15 drops daily given in divided doses before each feed. The patient failed to respond in 39% of cases and resort had to be had to surgery. In this series 6 (9%) died.

Grimes, Bell and Olney (1950) operated on 113 cases between 1930 and 1950 with no deaths. Browne (1951) reported a 2% mortality rate in 407 cases. Levi (1941) reported 100 consecutive operations on breast-fed babies without a death, though 11% of artificially fed infants died.

In a series of my own of 28 cases treated by pyloromyotomy, 13 infants were fed on the breast and 15 artificially; all recovered after the operation. It is certainly possible to recognize clinically those cases in which medical treatment may justifiably be tried for several days before recourse is had to surgery. The rule I adopted was to operate upon every case with a palpable pyloric tumour, and in the present series of 28 cases treated by pyloromyotomy, an immediate decision in favour of surgery was made in 24 cases, the remaining 4 cases being treated medically with either Eumydrin or Pylorostropin for 3-7 days before operation was decided upon.

It must be remembered that antispasmodic drugs such as Eumydrin and Pylorostropin, though capable of relieving pylorospasm, cannot directly affect the stenosis. The relative

importance of hypertrophy and spasm in any one case may vary, and thus if the latter predominates, improvement with eumydrin will follow; whereas if hypertrophy is the essential feature, only surgical intervention will relieve the obstruction. In this series a tumour was palpated in 22 cases (78%), whilst in 6 cases (22%) no tumour was palpable, but in the latter group the diagnosis was beyond doubt and on the operating table under anaesthesia the tumour was easily felt.

AETIOLOGY

Incidence. Infantile hypertrophic stenosis is a disorder with an incidence of 1 per 250 births. Wallgren (1941) assessed the frequency in Gothenburg as 4 per 1,000 live births, and Davison (1946) as 2.8 per 1,000 live births in Newcastle. It is the commonest condition requiring surgical attention in the first weeks of life.

Race. Ladd et al. (1946) as well as Mitchell-Nelson (1946) have attested to the rarity of this condition in the American negro, whilst a recent case report of pyloric stenosis in an African infant by Wilson and Gelfand (1955) has emphasised the relative rarity of this condition in the African. This rarity may be an expression of racial or genetic differences.

Familial Incidence. Cockayne and Penrose (1943) have suggested that the incidence of congenital hypertrophic pyloric stenosis is determined by a recessive gene. The role of genetic factors has also been emphasised by Carter and Savage (1951), who reported a family of 11 brothers and sisters, 5 of whom had children, and 4 of them a child with pyloric stenosis, diagnosis in each case being confirmed at operation. In the present series one infant had a paternal uncle who had required operative relief of a hypertrophic stenosis in infancy, and whose own first-born male child had undergone pyloromyotomy.

Twin Incidence. Sheldon (1938) found 23 pairs of twins in 1,000 cases of pyloric stenosis. One twin only was affected in each of 22 pairs, and in the remaining pair both were affected.

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Gynaec.

Cockayne and Penrose (1943) found 13 affected twins in 11 pairs among 449 cases. In this series 2 infants were each one of twins affected, the corresponding twin being unaffected. In these three series of cases out of 1,477 cases of pyloric stenosis 38 were one of twins, giving an incidence of 1 per 39. This may be expressed as ½ of a pair of twins per 39, thus giving the relative incidence of twins to non-twins as 1 per 78. As this is the same ratio as the incidence of twin births, it must be assumed that the occurrence in twins is a fortuitous one and should not be regarded as a manifestation of a genetic pheno-

Sex. In the present series 24 were males (86%), and only 4 were females. This is out of all proportion to the incidence of male to female births. It is in keeping with other reported series (Barrington-Ward, 1937, and Ladd et al., 1946), but no satisfactory explanation can be found for this overwhelming preponderance.

Age. The condition generally occurs in the first 12 weeks of an infant's life, but there may be an appreciable delay between the onset of symptoms and the time the infant is brought for treatment. Thus, in my series 8 were first seen at 6 weeks of age and 6 were brought for treatment at 4 weeks of age; 3 cases presented at 3 weeks, 3 at 5 weeks and 3 at 8 weeks; 4 cases were evenly distributed at 7, 9, 10 and 12 weeks. One case which is included in the 3-weeks age-group was delivered of an Rh-negative mother by Caesarean section 5 weeks prematurely, and successful operation was carried out technically at minus 2 weeks of age. One case presented with symptoms immediately after birth and was successfully operated on the 3rd day after birth.

Birth Order. It has been customary to regard first-born males as genetically more liable to this disorder, but in this series, 13 cases (46%) were first born, 12 cases (43%) were second born, and three cases (11%) were third born.

Feeding History. It is unlikely that the type of feed—breast or artificial-can have any effect on the incidence of hypertrophic pyloric stenosis. Jewesbury and Page (1937) reported a series of 144 cases of whom 80 were wholly breast-fed. Since then the feeding pattern has undoubtedly altered, and 15 cases (55%) of the present series were artificially fed.

PATHOLOGY

The pyloric tumour is a hard, olive-shaped mass which consists of a grossly hypertrophied circular muscle and which grates when cut with the knife. It is $1\frac{1}{2}$ inches long and $\frac{3}{4}$ inch in diameter, ending abruptly at the duodenal end and projecting slightly into its lumen. The duodenal mucosa is reflected off this projection and is liable to perforation at pyloromyotomy. In the pyloric region the muscular hypertrophy compresses the mucosa and throws it into longitudinal folds, aggravating the mechanical obstruction. The stomach proximal to the obstruction undergoes dilatation and suffers a variable degree of gastritis.

Pathogenesis. Numerous theories have been propounded in an attempt to explain the significance of the pyloric lesion, but the only two acceptable possibilities are that a congenital muscle hypertrophy or a neuro-muscular incoordination is the primary factor, the functional obstruction at the pylorus resulting in a compensatory hypertrophy of the muscle fibres of the pyloric canal.

In 12 cases of the series under report the Fredet-Rammstedt operation was modified so that a biopsy of the hypertrophied muscle and submucosa could be performed. Histological examination of this material disclosed no organic alteration in the normal neural pattern. It is thus highly probable that the primary lesion is a congenital muscle hypertrophy, the pyloric obstruction being due to the increased thickness of muscle, the mucosal compression, and a varying degree of spasm.

Donovan (1946) has indicated that there is no correlation between the age at which operation is carried out and the size of the pyloric tumour, and my impression confirms this. The degree of superimposed pylorospasm probably determines the time of onset of symptoms as well as their severity.

DIAGNOSIS

An infant who vomits regularly during or after feeds, who fails to gain weight and becomes constipated, and who on examination has demonstrable peristalsis and a palpable pyloric tumour, almost certainly has pyloric stenosis. The clinical presentation is not, however, always so classical, and analysis of the presenting features in the present series is not without interest.

Vomiting. In this series the duration of vomiting before treatment was commenced has varied between 2 days and 6 weeks. The longer the duration, the more forceful has the vomiting been, but in no more than half the cases was it projectile. Thus the diagnosis of hypertrophic pyloric stenosis does not necessarily depend on the physical nature of the vomit. Characteristic, however, is the absence of bile from the vomitus, and this feature is considered to be of diagnostic import. The same feature has also been encountered in oesophageal atresia, in duodenal atresia and in pylorospasm, but differentiation of these conditions from congenital pyloric stenosis has not been considered a difficult task.

Constipation. In all but 4 of the cases in this series constipation was present. In a 12-week-old infant with a 6 weeks history of vomiting, the bowels acted regularly despite its pale marasmic state and the presence of a distended stomach, peristalsis, and a palpable pyloric tumour. In the remaining 3 cases loose diarrhoeic stools were out of keeping with the usual picture of pyloric stenosis, but culture of the stools disclosed an associated Shiga enteritis probably engendered by the loss of gastric acid protection.

Failure to gain weight was a constant feature in all the cases in the present series. It is due to failure to maintain the child's nutrition and to some extent to dehydration.

Dehydration. Though a certain amount of loss of tissue turgor was present in all, only 6 cases were so dehydrated as to require parenteral fluid replacement.

Jaundice is an unusual feature in hypertrophic stenosis and was encountered once in the present series. referred to earlier, had been delivered by Caesarean section of an Rh-negative mother. Coombs test carried out on the childs serum was negative, while the blood picture was normal. Fouchet's test, however, was positive, whilst serumbilirubin estimations gave a total of 10.4 mg.%, of which 9.93% was obtained by the indirect quantitative assessment. The jaundice was more probably due to hepatic dysfunction resulting from vomiting in a premature infant than to haemolysis, for within 24 hours of pyloromyotomy the jaundice had completely resolved.

The exaggerated peristalsis of the stomach Peristalsis. proximal to the obstruction at the pylorus is always carefully looked for, and the administration of a feed of sweetened water may precipitate its appearance. This sign, however, is not invariable, and in the present series, though carefully

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looked for, was found in 21 cases (75%). In 2 cases, despite the absence of visible peristalsis, distension of the stomach was apparent.

Tumour. The presence of a palpable pyloric tumour is pathognomonic of hypertrophic pyloric stenosis, and is a strong indication for pyloromyotomy, but its absence does not invalidate either the diagnosis or the necessity for surgical intervention. Thus, despite experience in the palpation of the infant abdomen, the tumour was palpated clinically in only 21 cases (75%). The indications for Rammstedt's operation were, however, sufficiently strong to proceed to pyloromyotomy in the remaining 6 cases, and under the general anaesthetic the pyloric tumour was readily felt.

It is of interest to mention that in only 18 cases (64%) was the presence of a palpable tumour associated with visible peristalsis, whilst in 2 cases neither of these signs was discernible

Radiology. The essential radiological features consist of gastric dilatation, intermittent hyperperistalsis and the visualization of an elongated pyloric canal. Administration of a thin barium meal demonstrates a delayed emptying time, more than half the barium being retained in the stomach for 12 or more hours. Only infrequently will radiological examination be absolutely necessary; in this series it was carried out in 4 cases as a confirmatory measure.

TREATMENT

Medical Treatment. Non-operative measures are indicated in the absence of a pyloric tumour. A 0.6% alcoholic solution of Eumydrin is used, containing 0.1 mg. (1/750 gr.) per drop. Up to 15 drops a day, given in divided doses before each feed, may be required to relax the pylorus. They are best placed on the infant's tongue or gums, from where rapid absorption takes place. Failure to respond within 48 hours should cause one to re-assess the position.

Important ancillaries to drug treatment are the administration of thickened fluids, gastric lavage, and careful nursing, with the patient isolated from the general ward. Subcutaneous or intravenous administration of fluid may be indicated.

Surgical Treatment. The importance of pre-operative preparation of the infant cannot be sufficiently stressed. Gastric lavage reduces distension and facilitates handling of the stomach at operation. Hydration of the infant, when necessary, is best carried out by intravenous administration of Hartmann's solution or Ringer's lactate. Early decision to perform pyloromyotomy will reduce the number of patients who require fluid replacement. In the present series 6 cases required parenteral fluid, the rest being sufficiently well hydrated without it.

Anaesthesia. In 23 cases pyloromyotomy was performed under general anaesthesia and in 5 under local anaesthesia. My personal impression was that general anaesthesia permitted more rapid and comfortable completion of the operation than when local anaesthesia was used. The 'double induction' technique of general anaesthesia was used. Anaesthesia is maintained until the peritoneum has been opened, and during the subsequent surgical manoeuvres the infant is permitted to become 'light' until it is time to suture the peritoneum, when anaesthesia is re-induced. The average operating time in all these cases was less than 15 minutes, whereas under local anaesthesia the average time was half an hour. It has been argued that the first post-operative feed has to be delayed if general anaesthesia is used, but in this

series the first feed has never been delayed beyond 4 hours after operation. It has also been my impression that wound healing is better and quicker when general anaesthesia has been used.

Operation. Since the introduction of pyloromyotomy by Rammstedt in 1912, the operative results have shown steady improvement, so that under optimum conditions all should recover. In the present series this standard was achieved. The essential requisite of the operation is the incision of the pyloric musculature commencing 0.5 cm. short of the pyloro-duodenal junction and running in a gentle curve up on to the stomach wall. The incised muscle is then separated until the mucosa bulges freely through the muscular hiatus. The two hazards to avoid are the division of a serosal vessel and perforation of the mucosa at the end of the fornix round the cervix-like protrusion of the pylorus. The latter accident occurred in 3 cases, but its immediate recognition permitted transverse suture of the perforation without detriment to the post-operative course.

Either a high mid-line or paramedian trans-rectus incision was used in this series, and each layer was sutured separately upon closure of the wound. The total absence of wound dehiscence is attributed to this small point of technique.

Post-operative Course. Breast-fed infants were given small amounts of expressed milk within 6 hours of operation, and 4-hourly breast feeds were instituted as soon as possible. Artifically fed infants were put on a schedule which commenced with a drachm of glucose water. This was increased hourly so that a half-strength feed could be given in 12 hours, the infant graduating to a full-strength feed within 18 hours of operation. This pattern was varied in only minor degrees in this series, without a single case of postoperative gastro-enteritis. The absence of post-operative complications must be attributed to the high standard of nursing as well as to the routine administration of a 4-day course of parenteral penicillin after operation. The infants were discharged on the 7th day after operation, with the exception of 2 who were sent home on the 10th day because their condition made further dietary control necessary before they were restored to their mothers' care.

SUMMARY

The importance of surgical relief for congenital hypertrophic pyloric stenosis is emphasized, and the clinical features of this condition are analysed in the light of a series of 28 cases. The pathology of the condition is briefly described and also an investigation into the neuro-muscular pattern in the pyloric region in 12 cases, which favours the view that the condition is congenital. A preference for general anaesthesia is indicated and the scheme of post-operative management described.

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PANCREATICO-DUODENECTOMY

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Until 1935 carcinoma of the head of the pancreas, ampulla, duodenum and common bile-duct were for practical purposes considered to be inoperable by reason of their relatively inaccessible situation, and therefore to be treated by palliative procedures directed towards biliary drainage only.

The first successful pancreatico-duodenectomy was recorded by Kausch¹ in 1912. His patient died 7 months after the operation, following cholecystostomy performed for cholangitis.

Pancreatectomy having been performed for tumours productive of hyperinsulinism in the early nineteen-thrities, Whipple, Parsons and Mullins² proceeded with pancreatico-duodenectomy as a radical treatment for carcinoma of the ampulla of Vater. As a first stage they performed a cholecystogastrostomy and in the second stage they resected the duodenum together with the head of the pancreas. They ligated the duct of Wirsung and established continuity of the intestinal tract by performing a posterior gastro-enterostomy.

This operation was not free from complications such as cholangitis and biliary and pancreatic fistulae, and its disappointments did not encourage surgeons in Europe to adopt the procedure, until 1942 when Nuboer performed his first pancreatico-duodenectomy in a sufferer from carcinoma of the ampulla of Vater. He followed the technique of Kausch, and made an end-to-end anastomosis between the stump of the pancreas and the upper end of the jejunum, instead of closing off completely the cut end of the former without anastomosing it to the gastro-intestinal tract.

Efforts were made, especially in America, to find a solution to the multitude of problems which beset the operation. The work in this respect of Whipple,² Brunschwig,³ Orr,⁴ Cattell⁵ and many others, were of paramount importance, and by their efforts the operation of pancreatico-duodenectomy is today a more or less standardized procedure, differing only in minor respects at the various clinics. The indications for the operation have moreover been extended to include carcinoma of the head of the pancreas, the pancreatic part of the common bile-duct and the duodenum. Child⁶ gives a comprehensive description of the development of the operation.

Although the mortality of the operation has declined, no doubt owing to better anaesthesia, more adequate treatment of shock, and wider experience of pancreatectomy, the indications for this operation are by no means agreed upon. Thus the prognosis depends upon the site of the tumour. Walter Hess⁷ (1954) could find in the literature only 4 cases of carcinoma of the head of the pancreas who survived the operation for 5 years—a 2% 5-year survival rate. He compares with this figure the 33.1% 5-year survival rate after the radical extirpation of the head of the pancreas and the duodenum for ampullary carcinoma. He no longer performs the radical operation for carcinoma of the head of the pancreas. The site of the tumour is furthermore related to the operative mortality. Thus Cattell and Pyrtek⁸ report an operative mortality of 5% in cases operated on for ampullary carcinoma, as compared with 16.5% in cases of carcinoma of the pancreatic head.

The high operative mortality rate, and the low average

survival rate (11 months—Cattell and Pyrtek®) have caused many surgeons to regard the operation with disfavour when performed for cancer of the head of the pancreas, but Stafford, Trimble and Classen® argue that since the operative mortality reported for palliative shunts is not significantly lower than that for the radical operation, and since the survival time is at least equivalent to that for palliative procedures (which is given as 9 months by most authors), they feel justified in continuing to perform pancreatico-duodenectomy in suitable cases.

Although it is not intended to discuss the clinical picture fully, mention must be made of gastro-intestinal haemorrhage. In carcinoma of the duodenum, as might be expected, melaena is usually an early sign, and sometimes gives rise to massive haemorrhage. In contrast to this, melaena has not occurred in the cases of ampullary carcinoma, although occult blood in the faeces was present in most cases. Owing to its deep position, carcinoma of the head of the pancreas gives rise to occult blood in the faeces only after it has ulcerated through into the duodenum.

UTRECHT CASES

What follows is an analysis of the results of 24 consecutive pancreatico-duodenectomies performed at the University Clinic, Utrecht, Holland. Although this number of cases is too small for definite conclusions, it will be seen that the outcome closely follows the pattern of most published series.

Age and Sex. The average age was $60 \cdot 6$ years. The youngest patient was 40 years of age and the oldest 80. There were 18 males and 6 females.

Mortality. Six patients died as a result of the operation (25%), and, 8 of the survivors died later (all from metastases)

TABLE I. SURVEY OF LESIONS

Nature of Lesion		umber		rative aths	Patients still alive (years)							
		Cases	No.	%	5	3	1	3/4	1/4	1/12	Total	
Ampullary Carcinoma		11	3	27	1	1		_	1	-	3	
Carcinoma of head		7	1	14-3	_	_	-	1	1	2	4	
Carcinoma of bile duct		1	1	100	-	-	_	-	_	-	_	
Carcinoma of duodenum	n	2	1	50	-	_	-	_	-	-	-	
Benign conditions		3	0	0	-	1	2	-	_	-	3	

TABLE II. PATIENTS WHO SURVIVED THE OPERATION, BUT WHO HAVE SINCE DIED

Nature of Le.	sion			Survival period (months)									
				35	18	17	13	11	9	6	3	average	
Ampulla			* *	1	1	1	1	_	-	_	_	21 m.	
Caput			* *	-	_	_	-	-	_	1	1	6 m.	
Bile duct		* *		recent	-	_	-	-	-	_	_		
Duodenum			* *	-	-	-	-	- 1	1	-	-	11 m.	

Excluding benign conditions, it will be noted that all patients who lived for longer than 11 months after the operation had the resection done for ampullary carcinoma.

Operative Procedure

The one-stage procedure is preferred to the two-stage, which is performed only when the patient is too ill to undergo the radical operation, or when there is severe liver damage. In the latter event the first stage consists of the establishment of a biliary—intestinal anastomosis—usually a cholecystogastrostomy. In this connection it must be pointed out that

Moore and Younghusband¹⁰ perform a simple external cholecystostomy, which, they claim, facilitates the performance of the second stage.

Apart from rendering the radical part of the operation more difficult, the two-stage procedure has the objection that, following the initial biliary-digestive anastomosis, a carcinoma of the head of the pancreas may metastasize widely within weeks, thus rendering the performance of pancreatico-duodenectomy impossible at the time of the second laparotomy. 11, 12

As a preparation for operation, a high-protein, high-carbohydrate diet is given, as well as insulin if the patient is suffering from diabetes mellitus. Anaemia and electrolyte disturbance, if present, is corrected. To correct any prothrombin deficiency, vitamin K, at least 10 mg. daily, is given for at least 3 days before the operation. Vitamin-B complex and vitamin C are also given, and breathing exercises begun.

Chemotherapy is indicated to combat infection of the biliary passages, and also for sterilization of the colon, as it is sometimes necessary to perform a hemi-colectomy.

Immediately before the operation, the stomach is intubated and a blood transfusion started.

The incision used by Nuboer consists of a right subcostal incision, commencing below the xiphisternum and running in the direction of the iliac spine, so that it may be prolonged if necessary.

The liver is nearly always enlarged, and if the gall-bladder and common bile-duct are dilated, a careful inspection of the pancreas, duodenum and common bile-duct is indicated. For a systematic inspection of these structures it is necessary to detach the hepatic flexure of the ascending colon, and to mobilize the duodenum according to the method of Kocher. It is often necessary to open the duodenum for adequate inspection of the ampulla, and a frozen section is done in doubtful cases. The lower end of the common bile-duct should be explored for any tumour. Frozen section is not always helpful in carcinoma of the head, but if this structure is the seat of tumour formation, and the remainder of the pancreas and the biliary tracts are healthy, the tumour is nearly always carcinomatous.

The non-malignant conditions which have to be differentiated from carcinoma are simple tumours of the common bile-duct, pancreas and ampulla, as well as inflammatory conditions like chronic pancreatitis and papillitis stenosans. The last-mentioned condition is commonly associated with cholecystolithiasis or choledocholithiasis, and the inflammatory process may give rise to a palpable swelling, consisting of the intraduodenal portion of the common bile-duct, together with enlarged glands above the stenosis. The condition may also occur primarily in the absence of stone, and is therefore very easy to confuse with carcinoma.

To inspect the important blood-vessels, the right ends of the lesser and greater omenta are detached from their respective gastric curvatures, and the isthmus is inspected to ascertain whether the superior mesenteric vein has been involved by the tumour. If this vein has not been involved, then the stomach is drawn downwards and to the left, to explore the upper border of the pancreas.

The incision along the periphery of the duodenum is prolonged upwards into the hepato-duodenal ligament, and the latter is ligated and divided in portions from its lateral side, to isolate the common bile-duct. This should be done as low as possible to prevent injury to the hepatic

artery by pulling the duodenum downwards. When the common bile-duct is freed, the portal vein becomes visible. The peritoneum lining the posterior wall of the omental bursa is incised to isolate and inspect the hepatic artery and its branches. The gastro-duodenal artery is ligated where it leaves the hepatic artery.

After the stomach has been freed from its omental attachments on the greater and lesser curvatures, it is divided high up in the fundus, and the distal portion is displaced to the right, so that the whole of the pancreas lies exposed.

The gall-bladder is removed and the hepatic duct transected just above the entrance of the cystic duct.

Attention is now paid to the isthmus, which is separated from the superior mesenteric vein by passing a sound upwards between the two structures, so as not to injure the tributaries of the vein. The isthmus is divided, and all bleeding points tied, special care being taken not to occlude the pancreatic duct. The mesenteric, splenic and portal veins are now visible.

By retracting the head, a number of veins draining from it into the inferior mesenteric vein are exposed and ligated. Sometimes a vein is found which drains directly into the portal vein. It must be carefully ligated.

The posterior pancreatico-duodenal arteries are now ligated and divided, where they appear from behind the superior mesenteric vein. A dense layer of fibrous tissue has to be divided here and by maintaining continuous traction, the uncinate process together with the adjacent lymph glands are gradually exposed and mobilized.

The duodeno-jejunal flexure is now exposed, and the ligament of Treitz divided. It is easy to see which jejunal artery is to be divided in order to mobilize the flexure and a length of jejunum upwards behind the mesenteric vessels. The jejunum is now divided in a well-vascularized part, and the distal part of the stomach, the head of the pancreas, and the duodenum, including the duodeno-jejunal flexure, are now free to be removed.

In the reconstruction of the digestive tract, the upper end of the jejunum is drawn upwards behind the superior mesenteric vessels. Its open end is anastomosed to the stump of the pancreas, two rows of interrupted linen threads being used. At a distance of 10 cm. from this anastomosis, an end-to-side anastomosis is made between the hepatic duct and the jejunum, 3 rows of catgut stitches on atraumatic needles being used. The free edge of the mesentery is now stitched to the posterior abdominal wall, and the opening in the mesentery around the jejunal loop is closed.

Finally a posterior gastro-jejunostomy is performed, by bringing up a jejunal loop through an opening made in an avascular area of the mesocolon, the edges of which should be stitched around the stomach.

Two drainage tubes—one for the pancreatico-jejunal anastomosis and one for the biliary-intestinal anastomoses—are brought out through separate stab wounds in the side.

When there is no evidence of metastases, but the tumour has already involved adjacent structures, the operation may be extended to include total pancreatectomy, right hemicolectomy or resection of a length of superior mesenteric or portal veins—with either end-to-end anastomosis if the gap is small, or a porto-caval anastomosis if the gap is large.

Post-operatively, close attention is paid to the pulse rate and bloodpressure, and shock is guarded against by adequate blood pethid Con and w trolled cases,

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blood replacement. Oxygen is given when necessary and pethidine for pain.

Continuous gastric suction is maintained for some days, and water and electrolyte requirements are carefully controlled. In view of the hypoproteinaemia present in many cases, the blood sodium-chloride level is maintained on the low side to prevent oedema.

Antibiotics and vitamin K. are continued for some days, and the breathing exercises, commenced before operation are continued. Blood-sugar estimations are carried out during the first few days, but in most cases no diabetes mellitus will occur unless it has been present before the operation.

As soon as the gastro-intestinal tract resumes its function. mouth feeds similar to those following partial gastrectomy are given.

The drainage tubes are shortened after the 5th day, and removed after a week.

Although the greater part of the stomach, the entire duodenum and the head of the pancreas have been removed. the majority of patients enjoy remarkably good health—free from major complaints or manifestations of physiological disturbances. Digestion of food is adequate, and the development of diabetes mellitus is rare-depending as it does on the efficiency of the pancreatic stump. The 3 patients who were operated on for benign conditions have all gained weight, and are in a fit state of health.

Few surgeons will dispute the value of pancreaticoduodenectomy for ampullary carcinoma. Hess reports a 5-year survival rate of 33.1% and Cattell one of 25%.

Although the results of the operation when performed for carcinoma of the head of the pancreas are disappointing, and although pancreatectomy for this condition has been abandoned by some surgeons, the majority still favour it, maintaining that, provided these cases can be operated on at an early stage, the possibility of a cure is always present. Eijsbouts12 (1956) has collected from the literature 12 cases who survived the operation for more than 5 years. Even if the operation is considered to be merely a palliative measure, it must be conceded that patients who have undergone the procedure described lead a more comfortable existence than those who have undergone palliative shunts like cholecysto-enterostomy and gastro-enterostomy. Moreover, many statistics show that the mortality after the radical operation is not considerably higher than that for the palliative measures. Thus Moore and Younghusband10 had a mortality of 38% in 29 cases of pancreatico-duodenectomy and a mortality of 27% in 18 cases who underwent shunts

OPSOMMING

Die resultate van 24 pancreatico-duodenectomieë uitgevoer aan die Heelkundige Universiteitskliniek, Utrecht, Holland, sowel as die operasie-tegniek word beskryf.

Alhoewel daar eenstemmigheid bestaan wat betref die behandeling van carcinoom van die papilla van Vater, is dit nog glad nie die geval wat betref kanker van die kop van die pancreas nie, en finale gevolgtrekkinge kan alleenlik gemaak word namate die resultate van groter series operasies beskryf word.

Ek wens langs hierdie weg my dank aan prof. J. F. Nuboer uit te spreek vir sy toestemming om hierdie resultate te publiseer, sowel as vir sy wenke en advies by die skrywe van hierdie artikel.

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A DEVICE FOR EXERCISING THE LEG MUSCLES

FRANK A. GOODLIFFE

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The importance of exercise in the treatment of muscles damaged by disease, and other causes, has long been recognized. The need of such exercise is heightened by the fact that the affected muscle will suffer further damage from disuse, presenting a formidable problem where the patient is confined to bed. There, immobilized, the patient has but slight opportunity and little incentive to move the lower limbs.

Aware of this problem and of the high incidence in poliomyelitis of damage to muscles moving the ankle and the knee, the author has sought means whereby these muscles can be freely and pleasurably exercised by the patient confined to bed, such patients usually being children, who are easily distracted. It seemed that such apparatus would involve a fairly complex mechanism if it were adequately to cover the full range of movements of the ankle and the knee, particularly so if (a) the mechanism were to include means for controlling the resistance to muscle action, and (b) if the patient's interest were to be captured by some visible effect from his activity and an appreciation of the progress made from day to day. This latter feature is of some psychological importance to the child patient whose interest can hardly be sustained without some element of entertainment.

Realising the impracticability for this purpose of purely

mechanical linkage involving pulleys, wires, rods and levers, I devised a simple alternative method of linking a pedal mechanism with a visual indicator interesting enough to encourage a child to persevere with the exercise prescribed. The choice lay between electrical, hydraulic and pneumatic means of operation, and the last was chosen on the grounds of its simplicity, lightness and resilience

At both the 'transmitting' and the 'receiving' end of the system, bellows were chosen in preference to the more expensive alternative of cylinders and pistons. Such bellows, with their attendant flexible tubes, are also being used in the construction of a variety of other exercisers already designed for the treatment of muscles.

The apparatus under description has been designed for use by the physiotherapist whose need to give selective and controlled exercise to specific muscles and muscle-groups of his patient's ankles has been fully provided for. Its use for a more limited exercise of the muscles of the knee is mentioned below.

THE APPARATUS: 'REHABILITATOR' (ANKLE)

This model (Fig. 1) is designed for the exercise of the ankles in various planes of movement, but the 'transmitting' component

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can be adjusted to involve, also, certain of the muscles of the knee. There are two completely independent pedals (Fig. 1), each with

adjustments for procuring the plane of movement desired.

By loosening the wing-nut (WN), the entire pedal unit may be tilted backwards or forwards (Fig. 2) and/or rotated around the axis of the fixed component of the pedal (Fig. 3).

A third adjustment around the major axis of the leg is attainable

when the clamping lever (CL1) has been loosened for that purpose

(Fig. 4).

A fourth adjustment permits the foot to be moved to a new
The clamming lever (CL2) is position along its own major axis. The clamping lever (CL2) is loosened for making the change (Fig. 5). With an increase in the distance between the axis of the ankle and the hinge of the pedal, an increased share of the exercise is taken up by the muscles of the knee.

Resistant Pressures

Pressure against the downward movement of the foot is achieved to varying degree either by restricting the air-flow at the restrictor (R) (Fig. 6) or by weights or springs applied to the 'receiver' bellows (Fig. 7).

Pressure against the upward movement of the foot is achieved by the simple means of rubber bands (RB) of selected strength, stretched between the screws provided on the pedal sides (Fig. 8).

Rate of Exercise

. An adjustment is provided to alter the rate of pedal-movement required to achieve a given response at the 'receiving' indicator. This consists of a valve (BV) which can be set to bleed off a proportion of the generated pressure (Fig. 9).

In the model under review, this 'valve' consists of no more than a threaded stem from which a taper has been filed. The progressive unscrewing of the stem allows a progressive increase in the volume of escaping air.

The Indicator

The rehabilitor here described is shown (Fig. 1) with an indicator expressly designed for the interest and encouragement of the younger patient. Here the reward for effort is the emergence from the waves of two colourful swimmers who then continue to 'tread water' for the duration of the exercise. Experience with this design has shown a definite reluctance on the part of the patient to cease pedalling and thereby to allow the swimmers to 'drown'.

The pneumatic principle has the advantage of enabling the ready attachment by flexible tubing of any other such indicators of varying complexity and interest.

Instruments for the more exact assessment of the patient's

condition and progress can also easily be attached.

Other Details

The arc of possible movement by the foot is limited by the length of the flexible strap (FS) (Fig. 10). This strap has since been lengthened and perforated to make this limit variable.

Designed mainly for the exercise of the patient in bed, the frame of the apparatus is fitted with soft cords of adjustable length

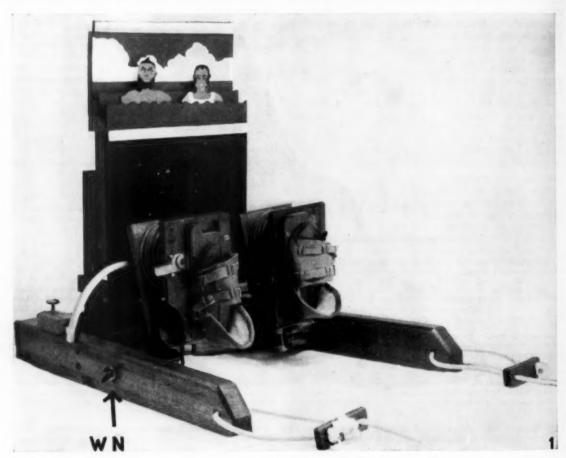


Fig. 1

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Figs. 2-13

(Fig. 1). This provides a firm anchorage when looped around the head-posts of the bed.

The soft leather sandals into which the feet are strapped are of two sizes. They provide a range of size for average patients of all ages. The sandals can be removed for changing by releasing the clamping lever CL1 (Fig. 11).

Provision is made, too, for increasing the distance between the pedals. This is done by loosening the central wing-nut (CWN), and then opening the frame about the hinge (H) (Fig. 10). The resulting slight change in the angles of the pedals can, if important, be corrected by the means already described.

Each bellows unit is built up from a series of flexible 4-inch discs having a central circular 1-inch hole. The discs are cemented alternately around their outer and inner edges, using a pliable adhesive. For the pedal bellows leather is chosen for its high durability, whilst for the indicator bellows, which are subjected to less wear, rubber sheeting is considered to be adequate.

The inlet and outlet valves of the pedal bellows each consist of a small leather flap which, while permitting air to flow in one direction, prevents its return by sealing off the hole through the tube on which it rests. A valve (FV) has been exposed by the removal of its cover (Fig. 9). It will be seen that the flap has been slotted to give it greater flexure.

In Fig. 9 is also shown the check (C) which, fixed within the valve casing, ensures that the flap is kept sufficiently close to its seating for instant closing when the direction of the air requires.

The author was encouraged during the latter stages of the development by the warm interest and help of Dr. J. J. Commerell, of Cape Town, and the guidance he gave in identifying by touch and sight the muscles selectively put in action by the apparatus in its experimental stages. If was encouraging, too, to have attention drawn to the unintentional ankle movement of an uninterested 4-year-old patient whose foot had been left attached to a disconnected pedal; for with the child's attention elsewhere, his action seemed completely automatic, stimulated solely by the pressure of the pedal.

The design, the method of construction and the materials used in this model were conditioned by the hope that, through grants by one or more public-spirited bodies, materials might be made available from which the apparatus might be produced by the collective craftsmanship of a sympathetic public. The additional photographs (Figs 12 and 13) showing some otherwise obscure details are here published to that end.

PROFESSORSHIP OF SURGERY, UNIVERSITY OF WITWATERSRAND

Mr. D. J. du Plessis, first assistant to the professor of surgery at the University of Cape Town and senior surgeon at Groote Schuur Hospital, Cape Town, has been appointed professor of surgery at the University of the Witwatersrand and chief surgeon on the

joint staff of the University and the Johannesburg General

Hospital. Mr. du Plessis, who will assume duty later this year, will occupy the post left vacant the resignation of Prof. W. E. Underwood in 1956.

Mr. du Plessis, who is 39, as educated at the Paarl was educated at the Paarl Boys' High School and became a student at the University of Cape Town where he qualified in medicine in 1941. He served his internship in military hospitals in Pretoria and Sonderwater and then became a medical officer in the 20th South African Field Ambulance



became a post-graduate student in surgery at the University of Cape Town. In 1948 he came to Johannesburg where he became surgical registrar at Baragwanath Hospital but after a year he returned to Cape Town where he became surgical registrar at Groote Schuur Hospital, a position he held for two years until he left for Britain in 1951 as holder of a Nuffield Scholarship. In the same year he was awarded the degree of Master of Surgery by the University of Witwatersrand for a thesis entitled 'A Clinico-Pathological Study of Mixed Salivary Tumours'.

Mr. du Plessis spent the next 18 months at numerous institutions in Britain, including the Oxford University Medical School, St. Mark's Hospital, St. Thomas' Hospital and St. James' Hospital, Balham. He is a Fellow of the Royal College of Surgeons, England

In June, 1952 he was appointed full-time lecturer and surgeon on the joint medical staff of the University of Cape Town and Groote Schuur Hospital and for the last 18 months he has been in charge of one of the three general surgical units in Groote Schuur Hospital. A year ago he was promoted to the highest grade on the joint medical staff. He has taken an active part in post-graduate training at the hospital and he has played a prominent part in re-organizing the Cape Town Blood Transfusion Service.

Mr. du Plessis has for the last 9 years been conducting clinical and histological research into diseases of the parotid salivary gland and several papers on the results of his work have already been published.



CAPE WESTERN BRANCH

It has recently been decided by Branch Council that a resume of proceedings at the monthly meetings be published in the Journal for the information of interested members. The following items of general interest were discussed at the most recent meeting of Branch Council held on 18 April 1958:

Annual Cape Western Branch Church Service: At the invitation of the Rector of St. Stephens Church, Pinelands, the Rev. Leslie A. Davis, members of the Association had been invited to attend a special service on St. Luke's day last year and the year before, at which the President had read the lesson. At the suggestion of our President, Dr. G. M. Malan, and as Mr. Davis had left for overseas, Branch Council decided that an annual service of this kind should be held in one or other of the Churches in the Peninsula of that particular denomination to which the President belonged. Arrangements will be made in due course for the first service of

this kind to be held soon in the Groote Kerk, Cape Town. This suggestion was received with enthusiasm by members of the Council, and it is hoped that many members of the Association will attend and will be looking forward in anticipation to a similar service next year at the Synagogue when Dr. Landau is President.

Income Tax Reductions for Medical Visits Overseas: In response to a recent notice circularized, enquiries have been received from several senior members of the profession which has exposed an important shortcoming in the regulations as they stand at the moment, according to which evidence has to be produced that the member who had been abroad had been engaged in post-graduate study. As more and more of the senior members of our medical schools are being invited overseas to teach at post-graduate courses, lecture at Congresses and demonstrate their surgical technique, thereby enhancing the reputation of our teaching establishments, it seems rather unfair that they should not be

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entitled to income tax relief in spite of the fact that they have to incur considerable expense to go and teach overseas instead of

It was moved that the Parliamentary Committee should be approached through Branch Council to suggest that this matter e remedied.

Shares in Medical Centre: The news that our 2,640 shares in Medical Centre had been sold at a very satisfactory premium, the profit being £330, was received from the Hon. Treasurer, Dr. J. K. de Kock, with general acclaim. It was agreed that the funds be invested with Federal Trust on a two-year fixed deposit at an interest of 6%

Traffic Committee: This Committee had been advised that the City Council had agreed to the issue of the special badges, a holder, copy of the regulations and a map, at a charge of £1.

The badges are being ordered and will be issued in the near future by the Traffic Department.

A motion of thanks to Dr. F. W. F. Purcell for his efforts in this matter was carried.

Medical House (Pty.) Limited: Dr. C. Shapiro has tendered his resignation as director, and Dr. J. K. de Kock, Hon. Treasurer of the Branch, was unanimously elected in his place.

First Congress of the S.A. Association of Surgeons: Prof. Jannie Louw cordially invited members to the first Congress held on 28, 29 and 30 April. It was reported that there would be some 60 surgeons present.

It is regretted that some of the more interesting procedures at Branch Council cannot be reported on in a resume intended for general circulation, but members are reminded that they are welcome to attend meetings of Council.

NEW PREPARATIONS AND APPLIANCES: NUWE PREPARATE EN TOESTELLE

MIDICEL TABLETS

Parke, Davis introduce Midicel, and supply the following information. It is a new long-acting sulphonamide which effectively combats many gram-negative and gram-positive bacterial infections. Clinical experience has demonstrated Midicel to be particularly appropriate in treating patients with infections of the genitourinary tract.

Midicel (sulphamethoxypyridazine, Parke-Davis) is chemically known as 3-sulphanilamido-6-methoxypyridazine, and is a sulphonamide which is rapidly absorbed and slowly excreted. In order to maintain adequate blood concentrations, conventional sulphonamide preparations require faithful adherence to a rigid dosage schedule—usually a dose every four or six hours. Such a burdensome schedule frequently results in omitted doses and consequent periods of low blood concentrations during which bacteria may again multiply. Midicel represents the fulfilment of a long quest in sulphonamide therapy—a safe, rapidly absorbed, long-acting antimicrobial agent that provides a sustained therapeutic effect with low oral dosage. A single daily dose provides effective blood levels for more than 24 hours, eliminating the hazard of blood 'fall-off' due to the omitted dose.

Indications. Evidence to date indicates that Midicel is clinically effective in a variety of infections responsive to sulphonamide therapy. These include respiratory infections, genito-urinary tract infections, but a backers, bacterial dysentery, rheumatic fever, and asymptomatic bacilluria in pregnant women. In the last two indications, Midicel has been employed prophylactically. The fact that Midicel is only moderately acetylated and slowly excreted by the kidneys, together with its high solubility at the acid pH commonly observed in kidney infections, adequately explain its effectiveness in genito-urinary tract infections, due to E. coli, Aerobacter aerogenes streptococci, staphylococci, gram-negative bacilli, d phtheroids, and some cases of proteus infection.

Dosage and Administration. As Midicel produces prolonged effective levels in the blood it requires only a fraction of the dosage usual for most sulphonamides. The adult dose in mild to moderately severe infections is 2 tablets (1 g.) the first day, then moderately severe infections is 2 tablets (1 g.) the first day, then 1 tablet (0.5 g.) daily, or 2 tablets every other day. For severe infections, 4 tablets (2 g.) the first day, then the usual 1 tablet (0.5 g.) daily is recommended. Children require dosage in proportion to body-weight: for each 20 lb. \(\frac{1}{2}\) tablet (0.125 g.)—6.25 mg. per lb. body-weight—the first day; then \(\frac{1}{2}\) tablet (0.0625 g.)—3.12 mg. per lb. body-weight—daily. Because of slow excretion rates and prolonged blood levels, it is recommended that this dosage should not be exceeded. Continue for 5-7 days or

until patient is free of symptoms for 48-72 hours.

Precautions. Side-effects common to the sulphonamides in general may sometimes occur with Midicel. These include headache, malaise, anorexia, skin rash and drug fever. Owing to low dosage and low concentration in the healthy kidney, crystalluria is unlikely, but adequate fluid intake should be maintained during and for at least 24-48 hours after treatment. Patients with impaired renal function should be followed closely since excessive

accumulations of the drug may occur.

Package. Quarter-scored tablets of 0.5 g. in vials of 12 and Package. Q bottles of 100.

- Ross, S., Ahrens, W. E. and Zaremba, E. A. (1957): Ann. N.Y. Acad. Sci., 69, 501.
 Frisk, A. R. and Wassen, A. (1957): Antibiotics Annual, 1956-57, p. 424. New York: Medical Encyclopedia, Inc.
 Jackson, G. G. and Grieble, H. G. (1957): Ann. N.Y. Acad. Sci., 69, 493.
 Jones, W. and Finland, M. (1957): Ibid., 69, 473.
 Waiker, W. F. and Hamburger, M. (1957): Ibid., 69, 509.
 Lepper, M. H., Simon, A. J. and Marienfeld, C. J. (1957): Ibid., 69, 485.

PASSING EVENTS: IN DIE VERBYGAAN

Dr. W.F. Exner Baumann, accompanied by Mrs. Baumann has gone overseas on a three months trip. While abroad he will visit hospitals and clinics on the Continent and in the UK. *

Mr. Martin Singer has changed his residential address to 7 Beach Road, Muizenberg, Cape, where his new telephone number is 8-7695. His address and telephone numbers (3-2833 and 2-7712) at his consulting rooms, 909 Norwich House, Heerengracht, Cape Town, remain unchanged.

Dr. Gavin Hildick-Smith who from 1948 to 1950 served at the Baragwanath Hospital and the Infectious Fevers Hospital in Johannesburg, has been appointed Associate Director of Clinical Research for Johnson and Johnson at their Research Centre in New Jersey, U.S.A.

The Retreat Hospital Association (W.O. 2140) would greatly appreciate gifts of any medical equipment suitable for use in their dispensary and gastro-enteritis drip clinic. Also gifts of sample medicines etc. There is an urgent need for an accurate baby scale to weigh under-nourished babies. Enquiries: P.O. Box 49, Wynberg; Phones 76476, 73864.

Cape Town Paediatric Group. The next meeting of the Cape Town Paediatric Group will be held on Tuesday 6 May 1958 in the Lecture Theatre, Red Cross War Memorial Children's Hospital, Rondebosch, at 8.15 p.m. Prof. F. J. Ford, Head of the Department of Child Health, Univertsiy of Cape Town, will speak on: 'The Premature Infant'.

Research Forum. The next meeting of Research Forum, University of Cape Town, will be held in the A-Floor Lecture Theatre, Groote Schuur Hospital, Cape Town, on Wednesday 7 May at 12 noon. Speakers: Dr. H. Gordon, Mr. J. Wilkens and Prof. J. F. Brock. Subject: 'The effect of various dietary factors on the serum-cholesterol level and the faecal fat content.'

Members are reminded that they should notify any change of address to the Secretary of the Medical Association of South

Africa at P.O. Box 643, Cape Town as well as to the Registrar of the South African Medical and Dental Council, P.O. Box 205, Pretoria. Failure to advise the Association can only result in non-delivery of the *Journal*. This applies to members proceeding overseas as well as to those who change their addresses within the Union.

REVIEWS OF BOOKS: BOEKRESENSIES

HYPNOSIS

General Techniques of Hypnotism. By Andre M. Weitzenhoffer, Ph.D. Pp. xvi + 460. 24 Figures. \$11.50. New York and London: Grune & Stratton, Inc. 1957.

Contents: Preface. Acknowledgment. Part I. Foundations. 1. Preliminary Remarks. 2. Dynamics of Hypnosis. Part II. Waking Suggestions. 3. Preliminary Exercises and Demonstrations in Waking Suggestions. 4. More Waking Suggestions. 5. Practical Considerations Concerning Suggestions in General. Part III. Hypnosis and Hypnotic Suggestions. 6. Hypnotic Susceptibility and the Depth of Hypnosis: 1. Advanced Techniques. 9. The Induction of Hypnosis: III. Miscellaneous Methods. 10. Self-Suggestion and Self-Hypnosis: 11. States of Immobilization ('Animal Hypnosis'). 12. Hypnotic Phenomena: I. Principles and Simple Demonstrations. 13. Hypnotic Phenomena: II. Specialized Advanced Techniques. 14. Special Problems of Hypnosis. 15. Applications of Hypnotism. Part IV. Appendix.

It is over 50 years since Janet wrote on hypnosis in his *Psychological Healing*, and those chapters still remain the best review of the subject. Janet had extensive practical experience of hypnosis; he knew its dangers, difficulties and limitations, and he approached the matter with a clear and detached scientific outlook. Few have done so since then.

Dr. Weitzenhoffer has written a long book; he has reviewed the more recent literature extensively, particularly the psychoanalytical writings, and he makes no extravagent claims, but one feels that he has not been critical enough about the applications of hypnosis and the results of its use in psychological disorders. Furthermore it is a great pity that he has not made more use of controlled experiments, writing as he does from a centre for advanced studies at a university. It is surprising to find no reference at all to electroencephalographic studies of hypnosis, and there is a very disappointing section on 'animal hypnosis', which really explains nothing.

With the thoroughness of American Ph.D. writers he lists all the known techniques for inducing hypnosis, often with diagrams which are redundant for all except those who are devoted to the comic strip. However, for those who wish to try hypnosis for themselves the methods are clearly laid out, even though the prose is desperately heavy. Here, for instance, is a sample: 'A suggestion is a stimulus in the form of a meaningful statement or gesture (sign) made by one individual, the suggester, and directed at another, the suggestee, such that the idea or group of ideas it evokes initiates alterations of mental processes or of behaviour in the suggestee in the absence of conscious, volunatry participation and such that these alterations are neither innate nor acquired "normal" (adequate) responses to this stimulus.' The danger is that after a number of pages of such stuff the reader becomes a readee and falls into a deep uncritical trance.

However we must not lose sight of the fact that Dr. Weitzenhoffer's book is devoid of emotional claims, and is a serious attempt to describe what its title implies, and is to be welcomed on these grounds.

J.M.

VASCULAR CHANGES IN THE CEREBRAL ARTERIES

Die Vaskulären Erkrankungen im Gebiet der Arteria Vertebralis und Arteria Basialis. Von Prof. Dr. H. Krayenbühl und Dr. M. G. Yasargil. VIII, 170 Seiten, 125 Abbildungen in 205 Einzeldarstellungen, Lex.-8°, Ganzleinen DM 77.-. Stuttgart: Georg Thieme Verlag. 1957.

Inhaltsverzeichnis: Vorwort. Einleitung. Kapitel I: Embryologie. Kapital II: Anatomie der A. vertebralis. A. basialis und ihrer Äste. Kapitel III: Die Symptomatologie der Gefährerschlüsse im subtentoriellen Gebiet. Kapitel IV: Angiographie.

The authors devote the first two chapters to a detailed description of the embryology and the topographical anatomy of the vertebral and basilar arteries. The variations which occur in these arteries and their branches are very lucidly dealt with by the use of many

excellent diagrams. They then describe the neurological deficit caused by thrombosis in these arteries, and rightly come to the conclusion that an attempt to attribute a certain set of symptoms to an occlusion of one particular branch is not logical. They go on to discuss the vertebral angiography for the diagnosis of aneurysms of these arteries and their branches.

Although they realise that a very small percentage of these aneurysms are amenable to surgery, the main object in advocating vertebral angiography is to differentiate between a large aneurysm and a tumour.

As regards the arteriovenous malformations—of which there are many excellent reproductions—the main indication is to determine to what extent the malformations, which may be supplied by both carotid and vertebral systems, are supplied by the latter. This will influence the surgical approach to these malformations.

This book undoubtedly shows that a lot of information can be gained from the vertebral angiography which may influence the neurosurgical approach.

The technical difficulties and the complications are not discussed, but these factors should be considered in the indication of performing vertebral angiograms. One must bear in mind that the majority of vertebral angiograms give theoretical information rather than being practically valuable.

This book is well written and has excellent reproductions of vertebral angiograms. The bibliography is very extensive and complete. As it is one of the few books which deal adequately with pathology in the vertebral system, it will be of great interest to neurologists and neurosurgeons.

CANCER MANAGEMENT

The Biologic Basis of Cancer Management. By Freddy Homburger, M.D., forewords by Lauren V. Ackerman, M.D., Clarence Cook Little, Sc.D., Alton Ochsner, M.D. Pp. xviii + 354. 39 Tables. 10 Figures. \$10.00. New York: Paul B. Hoeber Inc. 1957.

Contents: Forewords. Preface. List of Tables. List of Figures. Part 1. The Etiology of Cancer. 1. Occupational and Environmental Causes of Cancer in Man. Experimental Carcinogenesis. 3. The Role of Heredity in the Causation of Cancer. 4. The Role of Viruses in the Causation of Cancer. 5. The Role of Hormones in the Causation of Cancer: 1. Experimental Aspects. Part 11. The Biologic Behavior of Cancer. 7. Host and Tumour Interrelations in Human Beings. 8. Host and Tumour Interrelations in Animals. 9. The Characteristics and Clinical Course of Cancer. 10. The Natural Behavior of Cancer in Animals. 11. The Chemistry of Tumors. Part 111. The Diagnostic of Cancer. 12. Pathology. 13. Cytology. 14. Other Diagnostic Procedures. Part IV. The Treatment and Prevention of Cancer. 15. Principles of Surgery. 16. Principles of Radiotherapy. 17. Principles of Chemotherapy. 18. Prevention of Cancer. Epilogue. References. Index.

The title of this book is rather optimistic. Every worker on the cancer problem will agree with the author that there is a wide gap between the new fundamental discoveries and their application in cancer prevention and treatment. There also is a lack of understanding between the various disciplines that concentrate their efforts on the cancer problem. In fact this is so much so that although the biological understanding of various aspects of malignant growth has advanced considerably, we are still far away from a well founded biological treatment of the disease.

Part 1 and Part 2 of this work are devoted to the fundamentals of the biology of cancer; Part 3 and Part 4 to what might be called the medical side of the problem. Most medical men who are experts in surgical, radiotherapeutic or chemotherapeutic methods of treatment of cancer, have little knowledge of what is being done in scientific research on the metabolism, growth and development of malignant cells, whereas most scientists engaged in cancer research have only a hazy notion of the pathology and clinical course of the disease.

The book under review may help to bridge this gap. It is written in an easily understandable style and offers an excellent introduction

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into various branches of cancer research to the medical man who wants to be aware of what is being done in fields other than his For this purpose the work can be strongly recommended, and will be appreciated by medical readers. However, it might have been desirable to devote more space to biochemical research with an introduction on cell metabolism understandable to the medical man with only an elementary knowledge of chemistry.

INDUSTRIAL TOXICOLOGY

Industrial Toxicology. 2nd Edition. By Lawrence T. Fairhall. Pp. xii + 376. 80s. Baillière, Tindall and Cox Ltd. 1957.

Contents: Preface. Introduction. Part I. Inorganic Substances. Part II. Carbon Compounds. Appendix. Index.

Compounds. Appendix. Index.

This book was one of the first publications to provide in a single compact reference work much of the important information on industrial toxicology. In this edition there is a completely revised digest of knowledge in this field. The great advances in chemical technology, the manufacture of so many new chemical substances and further data on toxic substances have necessitated many changes and the inclusion of new sections and new material.

The text is divided into two main groups increase substances.

The text is divided into two main groups inorganic substances (79 headings) and carbon compounds (181 headings). The substances are listed in alphabetical order in each group, and under each heading there is information on the characteristics, industrial uses, toxicity and analysis of the substance, and references to the literature. In the appendix are useful tables, for example, threshold limit values (the maximum average atmospheric concentration of contaminants to which workers may be exposed); the end products of detoxication of certain industrial compounds; the comparative toxicities of various substances.

The information provided in this book relates to the direct toxic effects of industrial poisons. The biological significance of the changes which foreign organic substances undergo in the body is not discussed in this work, a field of research that may give an insight into living processes in general.

This is a valuable book for those concerned with industrial

hygiene, but pharmacologists and medical practitioners also will find it useful as a source of information.

CLINICAL MEDICINE

Einführung in die innere Medizin. 6., erweiterte Auflage. Von Prof. Dr. H. J. Wolf. XX + 760 Seiten. 73 teils farbige Abbildungen. DM 39.80. Stuttgart: Georg Thieme Verlag.

Inhaltsverzeichnis: Vorworte. Einleitung. Der Krankheit bezriff. Allgemeines über die Infektion und über die Reaktionen des Organismus. I. Krankheiten der Atmungsorgane. II. Die Krankheiten des Mediastinums. III. Die Krankheiten des Herzens und des Kreislaufs. IV. Die Krankheiten des Blutes und der blutbildenden Organe. V. Die Krankheiten der Verdauungsorgane: Mund, Rachen, Speiseröhre, Magen, Darm, Bauchfell. VI. Die Krankheiten der Leber und der Gallenwege. VII. Die Krankheiten der Bauchspeicheldrüse. VIII. Die Stoffwechselkrankheiten. IX. Die Krankheiten der Drüsen mit innerer Sekretion. X. Die Störungen im Haushalt der Vitamine. XI. Die Krankheiten der Muskeln, Knochen und Gelenke. XIII. Die Infektionskrankheiten. XIV. Die parasitären Krankheiten des Menschen. XV. Vergiftungen. XVI. Interne Krebstherapie. Sachverzeichnis.

Like most good textbooks, the authors devote a good deal of the introductory chapter to the importance of thorough interroga-tion and the good relationship which must exist between doctor and patient. Equal emphasis is laid on meticulous observation as

and patient. Equal emphasis is laid on meticulous observation as regards clinical signs. Honesty is essential in coming to a bedside diagnosis. Special investigations must be regarded as an aid to the presumptive bedside diagnosis and not vice versa.

The different chapters proved to be of excellent standard and compatible with the teachings of British and American equivalents. The only difference is probably the generous prescription of arsenic preparations, something which has fallen into disuse in most other countries.

The section on heart and lung disease is appropriately combined with several X-ray photos and ECG tracings-very illustrative indeed.

In each case the histo-pathology is described, something which, although not essential, brings extra clarity and understanding. In summary one can say that this is one of those books where much is said in a few words with great effect.

The genesis, application and interpretation of ECG forms are discussed in conjunction with the various heart diseases.

Although nothing new is revealed, it nevertheless makes interesting reading for those who care to improve or refresh their medical repertoire.

The section on endocrines is very interesting and up-to-date. Unlike so many textbooks, most facts are given in tabulated form and the author seems to have no doubt about his facts. The anatomy and physiology of the supra-renals are described, and the influence of their hormones on body growth and the hypophysis is reviewed with special reference to hypo- and hyper-secreting

MEDICAL PARASITOLOGY

Medical Parasitology. Second Edition. By William G. Sawitz, M.D. Pp. ix + 342. 89 Figures. New York: McGraw-Hill Book Company, Inc. 1956.

Contents: Preface. Acknowledgements. Textbooks and Journals Important in Parasitology. Introduction. Classification of Parasites. 1. Protozoa: Intestinal Protozoa. Atrial Protozoa. Blood Protozoa. Haemofagellates, Haemosporidia. Toxoplasma. 2. Helminths; Nemathelminthes or Roundworms. Nematoda. Platyhelminthes or Flatworms: Cestoda or Tapeworms, Trematoda or Flukes. 3. Arthropoda; Chilopoda, Crustacea, Arachinda, Insecta. 4. Treatment: Protozoan Infections. Helminthic Infections. Arthropod Infestations. Insecticides. 5. Synopsis. 6. Techniques for Laboratory Diagnosis. Vocabulary of Technical Terms. Index.

Medical Parasitology is a subject about which all too many general practitioners and physicians will readily admit their ignorance having spent, as a rule, the irreducible minimum of time in develop-

ing an acquaintance but seldom an appreciation of it.

This second edition of Medical Parasitology by the very well This second edition of Medical Parasitology by the very well known William G. Sawitz is the answer to the requirements of medical students, general practitioners and physicians. Added to these should be all medical laboratory workers who are not already specialists in this field. Not only does this book cover in synoptic, yet eminently readable, fashion what is important among the protozoa, helminths and arthropoda for the medical man but there is in addition. is, in addition, a section on the treatment of the diseases they cause which is up-to-date and most valuable.

The book is designed for easy reference and comprehension and numerous excellent illustrations facilitate this. Altogether it is a most attractive publication and no practitioner should be without

A.K.

CELLULAR CHEMISTRY OF NEURAL TISSUE

Ultrastructure and Cellular Chemistry of Neural Tissue. Edited by Heinrich Waelsch, M.D. Pp. xi + 249. Figures 40. \$7.50. New York: Paul B. Hoeber, Inc. 1957.

New York: Paul B. Hoeber, Inc. 1957.

Contents: List of Participants. Introduction. Acknowledgments. I. Some Aspects of The Ultrastructure of Double Membranes. II. The Fine Structure of the Neurophypophysis. III. Abnormal Metachromatic Lipids in Diffuse Sclerosis and Other Conditions. IV. Quantitative Analysis of Single Nerve Cell Bodies. V. In Vitro Studies on the Growth Properties of Brain Cortex Cells of Adult Individuals. VI. The Cell Density of Neural Tissues: Direct Cour ting Method and Possible Applications as a Biologic Referent. VII. Barbiturates and Certain Aspects of Phosphorus Metabolism in the Central Nervous System. VII A. Effect of Chlorr romazine on Oxidative Phosphorylation of Liver and Brain Mitochomdria. VIII. The Localization of Acetylcholinesterase in Neurons. IX. Histochemical Studies of the Esterases of Human Sympathetic Ganglia. X. Quantitative Histochemistry of Proteolytic and Oxidative Enzymes in Human Cerebral Cortex and Brain Tumors. X. A. Blood-Brain Barrier and Protein Turnover Studied with the Aid of Isotopic Lysine. XI. The Quantitative Distribution of Eight Enzymes of Glucose Metabolism and Two Citric Acid Cycle Enzymes in the Cerebellar Cortex and Its Subjacent White Matter. XI A. Composition of the Particulate Matter of Cerebral Cortex During Development. XII. Television Scanning Microspectrophotometry. Index.

This book is of interest to the anatomist, physiologist hiochemist

This book is of interest to the anatomist, physiologist, biochemist and neuro-pharmacologist; the neurologist, unless he is engaged in research of this kind, would probably prefer to wait until this complicated field is further elucidated. From the viewpoint of neurophysiology this book is welcomed, not only because it deals with a difficult subject in a clear and careful manner but also because it fills again the field of neuroanatomy and physiology. because it fills a gap in the field of neuroanatomy and physiology.

As biochemists have concentrated on the elucidation of the metabolism of muscular and connective tissue, so have anatomists and physiologists, but neural tissue has been somewhat neglected. This is not surprising as its function and composition is most difficult to understand.

Up to now little was known about the fine structure of the neurohypophysis and little about ultra-structure of double membranes. In this book the latter has been dealt with most interestingly by J. D. Robertson (Chapter I), and the former by Sanford L. Palay (Chapter 2).

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Since von Muralt wrote about growth factors derived from brain tissue (for speeding up the regeneration of nerves—an investigation which apparently did not fulfil its promise) the problem of growth properties of brain nerve cells has become of increasing interest to scientists. R. S. Geiger in his 'in vitro studies on the growth properties of brain cortex cells of adult individuals' (Chapter 5), deals not only with the morphology of neurons in culture but discusses the formation of synapses, the effect of sodium barbital in narcotic concentration, the effect of central-nervous-system stimulants such as pentylene-tetrazol (Metrazol) and the effect of electric stimulation. The changes of ultrastructure and function of brain tissue will be of especial interest, not only as a special field for the neurophysiologist and pharmacologist, but also to the neurologist-psychiatrist and the physicians.

MW

GREAT PHTHISIOLOGIST

Sir Robert W. Philip—1857-1939. Memories of his Friends and Pupils. Edited by Harley Williams. Pp. 96. 4 Illustrations. 12s. 6d. London: National Association for the Prevention of Tuberculosis. 1957.

Contents: Sir Robert Philip and the Edinburgh School of Medicine, by A. Fergus Hewat. Some Personal Recollections, by David P. Marais. My Predecessor in the First Chair of Tuberculosis, by Charles Cameron. The Story of the Tuberculosis Dispensary, by G. Lissant Cox. Pailip as a Teacher of Medicine, by Derrick Melville Dualop. Philip, The Clinician, by Christopher Clavon. Philip's Influence in Modern Social Medicine, by Donald Stewart. After Sir Robert Philip's Influence in Modern Social Medicine, by Donald Stewart. After Sir Robert Philip's Influence in Preventive Medicine, by Mahmoud Soliman Abaza. The Place of the Nurse in the Edinburgh Scheme, by Evolvenia Liston. Reminiscences of a Secretary, by Hilda Clark. A Visit to 43, Chylotte Square, by Harley Williams. Appendix I. Articles in Medical Literature by Sir Robert W. Philip. Appendix II. Syllabus of Professor Sir Robert Philip's Course on Tuberculosis in the University of Edinburgh.

This delightful little volume pays well-merited tribute to that great pioneer Phthisiologist the late Sir Robert Philip, in a manner that even Philip himself would have approved. The book is sponsored by the National Association for The Prevention of Tuberculosis to mark the centenary of Philip's birth. The various contributors were all connected with Philip either as friends, pupils or collaborators in his great crusade against Tuberculosis, first in Scotland and later in Great Britain. The development of the 'Edinburgh System' is traced, and in the light of modern control of Tuberculosis it makes very interesting reading. A very novel inclusion in a book of this nature is an Appendix which describes in detail the syllabus of Professor Sir Robert Philip's Course on Tuberculosis in the University of Edinburgh. Another appendix lists Philip's Articles in Medical Literature, more than 100 headings appearing in this

This book should be on the library shelves of every physician interested in Tuberculosis or in the History of Medicine.

A.I.

also included.

ARTIFICIAL INSEMINATION

Artificial Insemination in the Human. By A. M. C. M. Schellen, M.D., with an introduction by Sophia J. Kleegman, M.D. Pp. xii + 420. 10 Illustrations and 35 Tables. 72s. Amsterdam—Houston—London—New York: Elsevier Publishing Company. 1957.

Contents: Introduction. I. Nomenclature and Statement of the Problem. 2. The History of Artificial Insemination. 3. The Problem of Sterility. 4. The Artificial Insemination of Farm Animals. 5. Indications for A.I.H. and A.I.D. 6. Contra-indications. 7. Pre-treatment Requirements. 8. Methodology and Technique. 9. Choice of Donor. 10. General and Special Steps to be Taken by the Physician in the Matter of A.I.D. 11. Results. 12. Risks in a General Medical Sense Incident upon Artificial Insemination and its Irresponsible Application. 13. Adoption and A.I.D. 14. The Effect of the Publicity given to A.I. upon Public Opinion. 15. The Social and Economic Aspects. 16. The Psychological Aspects of A.I.D. 17. The Legal Problem of A.I. 18. The Moral and Religious Aspects of A.I.D. 19. Epilogue. Additional Bibliography. Subject Index.

Recently the Subject of 'Babies to Order and Phantom Fathers' has received a great deal of press publicity; no doubt this will result in the lay public seeking further information on the subject. Thus it is that the book by Dr. Schellen on 'Artificial Insemination in the Human' is as timely as it is a veritable gold mine of information. Dr. Schellen has produced an excellent treatise on this highly specialized subject, well documented and quite objective. He discusses the subject from all its aspects, moral, social, economic as well as the history and all its implications. He deals fully with technique and the law as it, applies to insemination in various countries. He also takes into account the theological aspects as it affects the various religious denominations. Dr. Schellen had

the opportunity of studying the use of the method on various clinics in the United States. In the States it is computed there are at least 100,000 donor babies.

It is clear that the author, while objective in his outlook, is himself convinced that insemination from donated semen is unjustified. Of particular interest are the Chapters on the social and moral implications and the psychological motives that impel people to seek artificial insemination.

G.I.

RENDICONTI ISTITUTO SUPERIORE DI SANITÀ

Rendiconti Istituto Superiore Di Sanità. Volume XVII. English Edition. Special number on pilot plant techniques of submerged fermentation. Edited by E. B. Chain, F.R.S. Pp. X + 243. Illustrated. Rome: Fondazione Emanuele Paterno. 1954.

Contents: Aeration Studies. A laboratory fermenter for vortex and sparger aeration. Fermenters of 90 and 3001, capacity for vortex and sparger aeration. A 'compensated' stuffing box and bearing unit for fermenters of semi-industrial and industrial capacities. Pilot plant for fermentation in submerged culture. A simple rotary shaker. Antifoam agents in aerobic fermentations. Evaluation of the activities of antifoam preparations. Interrelation of protein and polynucleotide synthesis in 'Escherichia coli'. The efact of mechanical agitation on the morphology of 'Penicillium chrysogenum'. Intereor is strictly fermenters. Romanoa, a new genus of soil fungus with antibacterial activity. Genetics of Penicillium chrysogenum'. I. Heterokaryosis in 'Penicillium chrysogenum'. Genetics of 'Penicillium chrysogenum'. II. Segregation and recombination from a heterozygous diploid.

The Instituto Superiore di Sanita must be congratulated for deciding to publish an English edition of its Journal and of the proceedings of symposia held under its auspices.

This volume, the first to be published in English, is mainly concerned with the bulk production of non-pathogenic microorganisms and describes the apparatus and technique used at the Institute for batches of up to 200 litres in enough detail for others to copy, adequate engineering drawings of all plant details being included. Some information about fermenters of 3,000 litre and 12,000 litre capacity is also given. Aeration, exclusion of contaminants, the suppression of foaming and the relation of these subjects to plant design are adequately discussed. The effects of agitation and culture volume on mycelial morphology are also briefly considered. It is to be hoped that the use of this plant for continuous culture will be described in a later publication.

Only a few unimportant mistakes were detected in the text and figures and the translation, considering the number of technical terms used, is very adequate.

Interesting microbial metabolism products are often formed in such exceedingly minute concentrations that the exciting new field which they represent can only be explored with the help of larger scale cultivation. The authors deserve thanks for assembling in one volume so much important information on this subject. Some interesting papers on more specialised microbiological subjects are

T.M.

STEDMAN'S MEDICAL DICTIONARY

Stedman's Medical Dictionary. 19th Revised Edition. Edited by N. B. Taylor, V.D., M.D., F.R.C.S., F.R.C.S. (Edin.), F.R.C.P. (Can.), M.R.C.S. (Lon.). Pp. xlvi + 1656. 88s. London: Baillière, Tindall & Cox, Ltd. 1957.

Contents: Preface. Key to the Pronunciation. Abbreviations Used in this Dictionary. How to Get Most Out of Your Dictionary. Medical Etymology. Dictionary of Medical Terms, A to Z. Appendix: Weights and Measures. Symbols. Stethoscopic Abbreviations. Proofreaders' Marks. Comparative Temperature Scales. Comparative Metric and English Barometer Scales. Chemical Elements. Important Microparasites Pathogenic for Man and Certain Animals. Nomenclature in Latin and English. Nomina Anatomica.

This dictionary which has now deservedly reached its 19th edition is one of the most valuable tools in the hands of the medical writer and journalist. Beautifully got up and illustrated with clear line drawings the book is a credit to the publishers, Messrs. Baillière, Tindall and Cox Ltd. and to the editor, Dr. N. B. Taylor. A number of new illustrations have been included and 'the names of pharmaceutical preparations have been changed from Latin to English in conformity with the latest editions of the United States and British Pharmacopoeias'.

An arduous duty has been well performed by the editors and the book must be found in every medical institute as well as on the desk of most medical authors. If an authoritative spelling or fact is required it is the last word.

T.S.

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